ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Humalog 100 units/ml solution for injection in vial
Humalog 100 units/ml solution for injection in cartridge
Humalog 100 units/ml KwikPen solution for injection in a pre-filled pen
Humalog 100 units/ml Junior KwikPen solution for injection in a pre-filled pen
Humalog 100 units/ml Tempo Pen solution for injection in a pre-filled pen

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains 100 units of insulin lispro* (equivalent to 3.5mg).

Vial

Each vial contains 1000 units insulin lispro in 10 ml solution.

Cartridge

Each cartridge contains 300 units of insulin lispro in 3 ml solution.

KwikPen and Tempo Pen

Each pre-filled pen contains 300 units of insulin lispro in 3 ml solution.
Each pre-filled pen delivers 1-60 units in steps of 1 unit.

Junior KwikPen

Each pre-filled pen contains 300 units of insulin lispro in 3 ml solution.
Each Junior KwikPen delivers 0.5 – 30 units in steps of 0.5 units.

*produced in *E.coli* by recombinant DNA technology.

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection.

Clear, colourless, aqueous solution.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

For the treatment of adults and children with diabetes mellitus who require insulin for the maintenance of normal glucose homeostasis. Humalog is also indicated for the initial stabilisation of diabetes mellitus.

4.2 Posology and method of administration

Posology

The dose should be determined by the physician, according to the requirement of the patient.

Junior KwikPen

Humalog 100 units/ml Junior KwikPen is suitable for patients who may benefit from finer insulin dose adjustments.

Humalog may be given shortly before meals. When necessary Humalog can be given soon after meals.

Humalog takes effect rapidly and has a shorter duration of activity (2 to 5 hours) given subcutaneously as compared with soluble insulin. This rapid onset of activity allows a Humalog injection (or, in the case of administration by continuous subcutaneous infusion, a Humalog bolus) to be given very close to mealtime. The time course of action of any insulin may vary considerably in different individuals or at different times in the same individual. The faster onset of action compared to soluble human insulin is maintained regardless of injection site. As with all insulin preparations, the duration of action of Humalog is dependent on dose, site of injection, blood supply, temperature, and physical activity.

Humalog can be used in conjunction with a longer-acting insulin or oral sulphonylurea agents, on the advice of a physician.

Special populations

Renal impairment
Insulin requirements may be reduced in the presence of renal impairment.

Hepatic impairment
Insulin requirements may be reduced in patients with hepatic impairment due to reduced capacity for gluconeogenesis and reduced insulin breakdown; however, in patients with chronic hepatic impairment, an increase in insulin resistance may lead to increased insulin requirements.

Paediatric population
Humalog can be used in adolescents and children (see section 5.1).

Method of administration

Subcutaneous use

Humalog preparations should be given by subcutaneous injection.

The KwikPen,Junior KwikPen and Tempo Pen are only suitable for subcutaneous injections. Humalog in cartridges is only suitable for subcutaneous injections from a Lilly reusable pen or compatible pump systems for continuous subcutaneous insulin infusion (CSII).

Subcutaneous administration should be in the upper arms, thighs, buttocks, or abdomen. Use of injection sites should be rotated so that the same site is not used more than approximately once a month, in order to reduce the risk of lipodystrophy and cutaneous amyloidosis (see section 4.4 and 4.8).
When administered subcutaneously care should be taken when injecting Humalog to ensure that a blood vessel has not been entered. After injection, the site of injection should not be massaged. Patients must be educated to use the proper injection techniques.

Humalog KwikPens
Humalog KwikPen is available in two strengths. The Humalog 100 units/ml KwikPen (and Humalog 200 units/ml KwikPen, *see separate SmPC)* delivers 1 – 60 units in steps of 1 unit in a single injection. The Humalog 100 units/ml Junior KwikPen delivers 0.5 – 30 units in steps of 0.5 units in a single injection. **The number of insulin units is shown in the dose window of the pen regardless of strength and no** dose conversion should be done when transferring a patient to a new strength or to a pen with a different dose step.

Humalog Tempo Pen
The Humalog 100 units/ml Tempo Pen delivers 1 – 60 units in steps of 1 unit in a single injection. The number of insulin units is shown in the dose window of the pen regardless of strength and no dose conversion should be done when transferring a patient to a new strength or to a pen with a different dose step. The Tempo Pen can be used with the optional transfer module Tempo Smart Button (see section 6.6).

As with any insulin injection, when using the Tempo Pen, Smart Button and the mobile application, the patient should be instructed to check their blood sugar levels when considering or making decisions about another injection if they are unsure how much they have injected.

Use of Humalog in an insulin infusion pump
For subcutaneous injection of Humalog using a continuous infusion pump, you may fill the pump reservoir from a Humalog 100 units/ml vial. Some pumps are compatible with cartridges that can be inserted intact into the pump.

Only certain CE-marked insulin infusion pumps may be used to infuse insulin lispro. Before infusing insulin lispro, the pump manufacturer's instructions should be studied to ascertain the suitability for the particular pump. Use the correct reservoir and catheter for the pump. When filling the pump reservoir avoid damaging it by using the correct needle length on the filling system. The infusion set (tubing and cannula) should be changed in accordance with the instructions in the product information supplied with the infusion set. In the event of a hypoglycaemic episode, the infusion should be stopped until the episode is resolved. If repeated or severe low blood glucose levels occur consider the need to reduce or stop an insulin infusion. A pump malfunction or obstruction of the infusion set can result in a rapid rise in glucose levels. If an interruption to insulin flow is suspected, follow the instructions in the pump product literature. When used with an insulin infusion pump, Humalog should not be mixed with any other insulin.

Intravenous administration of insulin

If necessary, Humalog may also be administered intravenously, for example: for the control of blood glucose levels during ketoacidosis, acute illnesses or during intra and post operative periods.

Humalog 100 units /ml is available in vials if administration of intravenous injection is necessary.

Intravenous injection of insulin lispro should be carried out following normal clinical practise for intravenous injections, for example by an intravenous bolus or by an infusion system. Frequent monitoring of the blood glucose levels is required.

Infusion systems at concentrations from 0.1 units/ml to 1.0 units/ml insulin lispro in 0.9% sodium chloride or 5% dextrose are stable at room temperature for 48 hours. It is recommended that the system is primed before starting the infusion to the patient.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

Hypoglycaemia.

4.4 Special warnings and precautions for use

Traceability

In order to improve the traceability of biological medicinal products, the name and the batch number of the administered medicinal product should be clearly recorded.

Transferring a patient to another type or brand of insulin

Transferring a patient to another type or brand of insulin should be done under strict medical supervision. Changes in strength, brand (manufacturer), type (regular/soluble, NPH/isophane, etc.), species (animal, human, human insulin analogue), and/or method of manufacture (recombinant DNA versus animal-source insulin) may result in the need for a change in dosage. For fast-acting insulins, any patient also on basal insulin must optimise dosage of both insulins to obtain glucose control across the whole day, particularly nocturnal/fasting glucose control.

Vial

When mixing Humalog with a longer acting insulin, the shorter-acting Humalog should be drawn into the syringe first, to prevent contamination of the vial by the longer-acting insulin. Mixing of the insulins ahead of time or just before the injection should be on advice of the physician. However, a consistent routine must be followed.

Hypoglycaemia and hyperglycaemia

Conditions which may make the early warning symptoms of hypoglycaemia different or less pronounced include long duration of diabetes, intensified insulin therapy, diabetic nerve disease or medications such as beta-blockers.

A few patients who have experienced hypoglycaemic reactions after transfer from animal-source insulin to human insulin have reported that the early warning symptoms of hypoglycaemia were less pronounced or different from those experienced with their previous insulin. Uncorrected hypoglycaemic or hyperglycaemic reactions can cause loss of consciousness, coma, or death.

The use of dosages which are inadequate or discontinuation of treatment, especially in insulin-dependent diabetics, may lead to hyperglycaemia and diabetic ketoacidosis; conditions which are potentially lethal.

Injection technique

Patients must be instructed to perform continuous rotation of the injection site to reduce the risk of developing lipodystrophy and cutaneous amyloidosis. There is a potential risk of delayed insulin absorption and worsened glycaemic control following insulin injections at sites with these reactions. A sudden change in the injection site to an unaffected area has been reported to result in hypoglycaemia. Blood glucose monitoring is recommended after the change in the injection site, and dose adjustment of antidiabetic medications may be considered.

Insulin requirements and dosage adjustment

Insulin requirements may be increased during illness or emotional disturbances.

Adjustment of dosage may also be necessary if patients undertake increased physical activity or change their usual diet. Exercise taken immediately after a meal may increase the risk of hypoglycaemia. A consequence of the pharmacodynamics of rapid-acting insulin analogues is that if hypoglycaemia occurs, it may occur earlier after an injection when compared with soluble human insulin.

Combination of Humalog with pioglitazone

Cases of cardiac failure have been reported when pioglitazone was used in combination with insulin, especially in patients with risk factors for development of cardiac heart failure. This should be kept in mind, if treatment with the combination of pioglitazone and Humalog is considered. If the combination is used, patients should be observed for signs and symptoms of heart failure, weight gain and oedema. Pioglitazone should be discontinued, if any deterioration in cardiac symptoms occurs.

Avoidance of medication errors

Patients must be instructed to always check the insulin label before each injection to avoid accidental mix-ups between the two different strengths of Humalog KwikPen as well as other insulin products.

Patients must visually verify the dialled units on the dose counter of the pen. Therefore, the requirement for patients to self-inject is that they can read the dose counter on the pen. Patients who are blind or have poor vision must be instructed to always get help/assistance from another person who has good vision and is trained in using the insulin device.

Tempo Pen

The Tempo Pen contains a magnet (see section 6.5) that may interfere with the functions of an implantable electronic medical device, such as a pacemaker. The magnetic field extends to approximately 1.5 cm.

Excipients

This medicinal product contains less than 1 mmol sodium (23 mg) per dose, i.e., essentially "sodium-free".

4.5 Interaction with other medicinal products and other forms of interaction

Insulin requirements may be increased by medicinal products with hyperglycaemic activity, such as oral contraceptives, corticosteroids, or thyroid replacement therapy, danazol, $beta_2$ stimulants (such as ritodrine, salbutamol, terbutaline).

Insulin requirements may be reduced in the presence of medicinal products with hypoglycaemic activity, such as oral hypoglycaemics, salicylates (for example, acetylsalicylic acid), sulpha antibiotics, certain antidepressants (monoamine oxidase inhibitors, selective serotonin reuptake inhibitors), certain angiotensin converting enzyme inhibitors (captopril, enalapril), angiotensin II receptor blockers, beta-blockers, octreotide or alcohol.

The physician should be consulted when using other medications in addition to Humalog (see section 4.4).

4.6 Fertility, pregnancy and lactation

Pregnancy

Data on a large number of exposed pregnancies do not indicate any adverse effect of insulin lispro on pregnancy or on the health of the foetus/newborn.

It is essential to maintain good control of the insulin-treated (insulin-dependent or gestational diabetes) patient throughout pregnancy. Insulin requirements usually fall during the first trimester and increase during the second and third trimesters. Patients with diabetes should be advised to inform their doctor if they are pregnant or are contemplating pregnancy. Careful monitoring of glucose control, as well as general health, is essential in pregnant patients with diabetes.

Breast-feeding

Patients with diabetes who are breast-feeding may require adjustments in insulin dose, diet or both.

Fertility

Insulin lispro did not induce fertility impairment in animal studies (see section 5.3).

4.7 Effects on ability to drive and use machines

The patient's ability to concentrate and react may be impaired as a result of hypoglycaemia. This may constitute a risk in situations where these abilities are of special importance (e.g. driving a car or operating machinery).

Patients should be advised to take precautions to avoid hypoglycaemia whilst driving, this is particularly important in those who have reduced or absent awareness of the warning signs of hypoglycaemia or have frequent episodes of hypoglycaemia. The advisability of driving should be considered in these circumstances.

4.8 Undesirable effects

Summary of safety profile

Hypoglycaemia is the most frequent undesirable effect of insulin therapy that a patient with diabetes may suffer. Severe hypoglycaemia may lead to loss of consciousness, and in extreme cases, death. No specific frequency for hypoglycaemia is presented, since hypoglycaemia is a result of both the insulin dose and other factors e.g. a patient`s level of diet and exercise.

Tabulated list of adverse reactions

The following related adverse reactions from clinical trials are listed below as MedDRA preferred term by system organ class and in order of decreasing incidence (very common: ≥1/10; common: ≥1/100 to <1/10; uncommon: ≥1/1,000 to <1/100; rare: ≥1/10,000 to <1/1,000; very rare: <1/10,000) ; not known (cannot be estimated form the available data).

Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.

MedDRA system organ classes	**Very common**	**Common**	**Uncommon**	**Rare**	**Very rare**	**Not known**
Immune system disorders						
Local allergy		X				
Systemic allergy				X		
Skin and subcutaneous tissue disorders						
Lipodystrophy			X			
Cutaneous amyloidosis						X

Description of selected adverse reactions

Local allergy

Local allergy in patients is common. Redness, swelling, and itching can occur at the site of insulin injection. This condition usually resolves in a few days to a few weeks. In some instances, this condition may be related to factors other than insulin, such as irritants in the skin cleansing agent or poor injection technique.

Systemic allergy

Systemic allergy, which is rare but potentially more serious, is a generalised allergy to insulin. It may cause a rash over the whole body, shortness of breath, wheezing, reduction in blood pressure, fast pulse, or sweating. Severe cases of generalised allergy may be life-threatening.

Skin and subcutaneous tissue disorders

Lipodystrophy and cutaneous amyloidosis may occur at the injection site and delay local insulin absorption. Continuous rotation of the injection site within the given injection area may help to reduce or prevent these reactions (see section 4.4).

Oedema

Cases of oedema have been reported with insulin therapy, particularly if previous poor metabolic control is improved by intensified insulin therapy.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V.

4.9 Overdose

Insulins have no specific overdose definitions because serum glucose concentrations are a result of complex interactions between insulin levels, glucose availability and other metabolic processes. Hypoglycaemia may occur as a result of an excess of insulin activity relative to food intake and energy expenditure.

Hypoglycaemia may be associated with listlessness, confusion, palpitations, headache, sweating and vomiting.

Mild hypoglycaemic episodes will respond to oral administration of glucose or other sugar or saccharated products.

Correction of moderately severe hypoglycaemia can be accomplished by intramuscular or subcutaneous administration of glucagon, followed by oral carbohydrate when the patient recovers sufficiently. Patients who fail to respond to glucagon must be given glucose solution intravenously.

If the patient is comatose, glucagon should be administered intramuscularly or subcutaneously. However, glucose solution must be given intravenously if glucagon is not available or if the patient fails to respond to glucagon. The patient should be given a meal as soon as consciousness is recovered.

Sustained carbohydrate intake and observation may be necessary because hypoglycaemia may recur after apparent clinical recovery.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group : Drugs used in diabetes, insulins and analogues for injection, fast-acting, ATC code: A10AB04

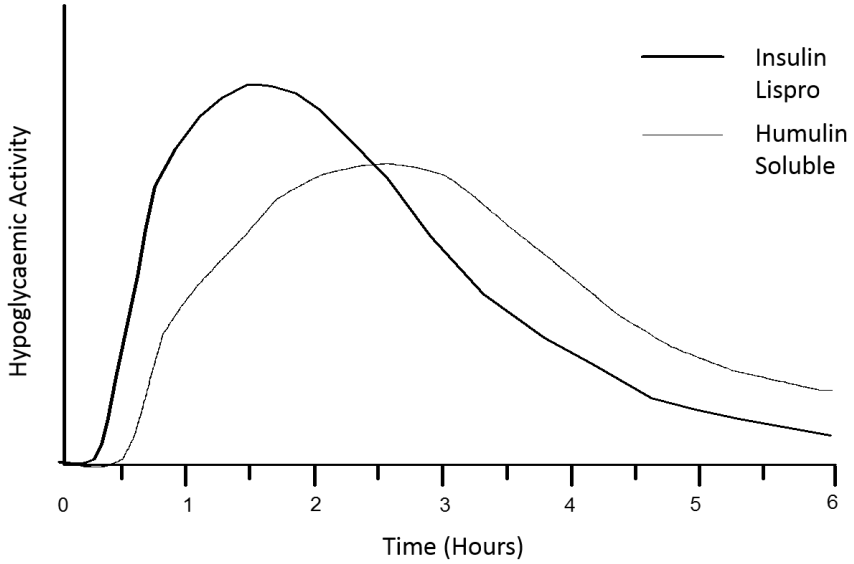
The primary activity of insulin lispro is the regulation of glucose metabolism.

In addition, insulins have several anabolic and anti-catabolic actions on a variety of different tissues. Within muscle tissue this includes increasing glycogen, fatty acid, glycerol and protein synthesis and amino acid uptake, while decreasing glycogenolysis, gluconeogenesis, ketogenesis, lipolysis, protein catabolism and amino acid output.

Insulin lispro has a rapid onset of action (approximately 15 minutes), thus allowing it to be given closer to a meal (within zero to 15 minutes of the meal) when compared to soluble insulin (30 to 45 minutes before). Insulin lispro takes effect rapidly and has a shorter duration of activity (2 to 5 hours) when compared to soluble insulin.

Clinical trials in patients with type 1 and type 2 diabetes have demonstrated reduced postprandial hyperglycaemia with insulin lispro compared to soluble human insulin.

As with all insulin preparations, the time course of insulin lispro action may vary in different individuals or at different times in the same individual and is dependent on dose, site of injection, blood supply, temperature and physical activity. The typical activity profile following subcutaneous injection is illustrated below.



The above representation reflects the relative amount of glucose over time required to maintain the subject's whole blood glucose concentrations near fasting levels and is an indicator of the effect of these insulins on glucose metabolism over time.

Clinical trials have been performed in children (61 patients aged 2 to 11) and children and adolescents (481 patients aged 9 to 19 years), comparing insulin lispro to human soluble insulin. The pharmacodynamic profile of insulin lispro in children is similar to that seen in adults.

When used in subcutaneous infusion pumps, treatment with insulin lispro has been shown to result in lower glycosylated haemoglobin levels compared to soluble insulin. In a double-blind, crossover study, the reduction in glycosylated haemoglobin levels after 12 weeks dosing was 0.37 percentage points with insulin lispro, compared to 0.03 percentage points for soluble insulin ($p = 0.004$).

In patients with type 2 diabetes on maximum doses of sulphonyl urea agents, studies have shown that the addition of insulin lispro significantly reduces HbA_{1c} compared to sulphonyl urea alone. The reduction of HbA_{1c} would also be expected with other insulin products e.g. soluble or isophane insulins.

Clinical trials in patients with type 1 and type 2 diabetes have demonstrated a reduced number of episodes of nocturnal hypoglycaemia with insulin lispro compared to soluble human insulin. In some studies, reduction of nocturnal hypoglycaemia was associated with increased episodes of daytime hypoglycaemia.

The glucodynamic response to insulin lispro is not affected by renal or hepatic function impairment. Glucodynamic differences between insulin lispro and soluble human insulin, as measured during a glucose clamp procedure, were maintained over a wide range of renal function.

Insulin lispro has been shown to be equipotent to human insulin on a molar basis but its effect is more rapid and of a shorter duration.

5.2 Pharmacokinetic properties

The pharmacokinetics of insulin lispro reflect a compound that is rapidly absorbed, and achieves peak blood levels 30 to 70 minutes following subcutaneous injection. When considering the clinical relevance of these kinetics, it is more appropriate to examine the glucose utilisation curves (as discussed in 5.1).

Insulin lispro maintains more rapid absorption when compared to soluble human insulin in patients with renal impairment. In patients with type 2 diabetes over a wide range of renal function the pharmacokinetic differences between insulin lispro and soluble human insulin were generally maintained and shown to be independent of renal function. Insulin lispro maintains more rapid absorption and elimination when compared to soluble human insulin in patients with hepatic impairment.

5.3 Preclinical safety data

In *in vitro* tests, including binding to insulin receptor sites and effects on growing cells, insulin lispro behaved in a manner that closely resembled human insulin. Studies also demonstrate that the dissociation of binding to the insulin receptor of insulin lispro is equivalent to human insulin. Acute, one month and twelve month toxicology studies produced no significant toxicity findings.

Insulin lispro did not induce fertility impairment, embryotoxicity or teratogenicity in animal studies.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

m-Cresol
Glycerol
Dibasic sodium phosphate. $7H_2O$
Zinc oxide
Water for injections
Hydrochloric acid and sodium hydroxide maybe used to adjust pH.

6.2 Incompatibilities

Vial

This medicinal product must not be mixed with other medicinal products except those mentioned in section 6.6.

Cartridge, KwikPen, Junior KwikPen and Tempo Pen

These medicinal products should not be mixed with any other insulin or any other medicinal product.

6.3 Shelf life

Before use

3 years.

After first use / after cartridge insertion

28 days.

6.4 Special precautions for storage

Do not freeze. Do not expose to excessive heat or direct sunlight.

Before use

Store in a refrigerator (2°C - 8°C).

After first use / after cartridge insertion

Vial

Store in a refrigerator (2°C - 8°C) or below 30°C.

Cartridge

Store below 30°C. Do not refrigerate. The pen with the inserted cartridge should not be stored with the needle attached.

KwikPen,Junior KwikPen and Tempo Pen

Store below 30°C. Do not refrigerate. The pre-filled pen should not be stored with the needle attached.

6.5 Nature and contents of container

Vial

The solution is contained in type I flint glass vials, sealed with butyl or halobutyl stoppers and secured with aluminium seals. Dimeticone or silicone emulsion may be used to treat the vial stoppers.

10 ml vial: Packs of 1 or 2 or a multipack of 5 (5 packs of 1). Not all packs may be marketed.

Cartridge

The solution is contained in type I flint glass cartridges, sealed with butyl or halobutyl disc seals and plunger heads, and are secured with aluminium seals. Dimeticone or silicone emulsion may be used to treat the cartridge plungers, and/or the glass cartridges.

3 ml cartridge: Packs of 5 or 10. Not all packs may be marketed.

KwikPen

The solution is contained in type I flint glass cartridges, sealed with butyl or halobutyl disc seals and plunger heads and are secured with aluminium seals. Dimeticone or silicone emulsion may be used to

treat the cartridge plunger, and/or the glass cartridge. The 3 ml cartridges are sealed in a disposable pen injector, called the “KwikPen”. Needles are not included.

3 ml KwikPen: Packs of 5 or a multipack of 10 (2 packs of 5). Not all packs may be marketed.

Junior KwikPen

Type I glass cartridges, sealed with halobutyl disc seals secured with aluminium seals and bromobutyl plunger heads. Dimeticone or silicone emulsion may be used to treat the cartridge plunger. The 3 ml cartridges are sealed in a disposable pen injector, called the “Junior KwikPen”. Needles are not included.

3 ml Junior KwikPen: Packs of 1 prefilled pen, 5 prefilled pens or a multipack of 10 (2 packs of 5) prefilled pens. Not all packs may be marketed.

Tempo Pen

Type I glass cartridges, sealed with halobutyl disc seals secured with aluminium seals and bromobutyl plunger heads. Dimeticone or silicone emulsion may be used to treat the cartridge plunger. The 3 ml cartridges are sealed in a disposable pen injector, called the “Tempo Pen”. The Tempo Pen contains a magnet (see section 4.4). Needles are not included.

3 ml Tempo Pen: Packs of 5 prefilled pens or a multipack of 10 (2 packs of 5) prefilled pens. Not all packs may be marketed.

6.6 Special precautions for disposal and other handling

Instructions for use and handling

To prevent the possible transmission of disease, each cartridge or pre-filled pen must be used by one patient only, even if the needle on the delivery device is changed. Patients using vials must never share needles or syringes. The patient should discard the needle after every injection.

The Humalog solution should be clear and colourless. Humalog should not be used if it appears cloudy, thickened, or slightly coloured or if solid particles are visible.

Do not mix insulin in vials with insulin in cartridges. See section 6.2.

Preparing a dose

Vial
The vial is to be used in conjunction with an appropriate syringe (100 unit markings).

i) Humalog

1. Wash your hands.

2. If using a new vial, flip off the plastic protective cap, but **do not** remove the stopper.

3. If the therapeutic regimen requires the injection of basal insulin and Humalog at the same time, the two can be mixed in the syringe. If mixing insulins, refer to the instructions for mixing that follow in Section (ii) and 6.2.

4. Draw air into the syringe equal to the prescribed Humalog dose. Wipe the top of the vial with a swab. Put the needle through the rubber top of the Humalog vial and inject the air into the vial.

5. Turn the vial and syringe upside down. Hold the vial and syringe firmly in one hand.

6. Making sure the tip of the needle is in the Humalog, withdraw the correct dose into the syringe.

7. Before removing the needle from the vial, check the syringe for air bubbles that reduce the amount of Humalog in it. If bubbles are present, hold the syringe straight up and tap its side until the bubbles float to the top. Push them out with the plunger and withdraw the correct dose.

8. Remove the needle from the vial and lay the syringe down so that the needle does not touch anything.

ii) Mixing Humalog with longer-acting Human Insulins (see section 6.2)

1. Humalog should be mixed with longer-acting human insulins only on the advice of a doctor.

2. Draw air into the syringe equal to the amount of longer-acting insulin being taken. Insert the needle into the longer-acting insulin vial and inject the air. Withdraw the needle.

3. Now inject air into the Humalog vial in the same manner, but do not withdraw the needle.

4. Turn the vial and syringe upside down.

5. Making sure the tip of the needle is in the Humalog, withdraw the correct dose of Humalog into the syringe.

6. Before removing the needle from the vial, check the syringe for air bubbles that reduce the amount of Humalog in it. If bubbles are present, hold the syringe straight up and tap its side until the bubbles float to the top. Push them out with the plunger and withdraw the correct dose.

7. Remove the needle from the vial of Humalog and insert it into the vial of the longer-acting insulin. Turn the vial and syringe upside down. Hold the vial and syringe firmly in one hand and shake gently. Making sure the tip of the needle is in the insulin, withdraw the dose of longer-acting insulin.

8. Withdraw the needle and lay the syringe down so that the needle does not touch anything.

Cartridge
Humalog cartridges are to be used with a Lilly reusable insulin pen and should not be used with any other reusable pen as the dosing accuracy has not been established with other pens.

The instructions with each individual pen must be followed for loading the cartridge, attaching the needle and administering the insulin injection.

KwikPen, Junior KwikPen and Tempo Pen
Before using the pre-filled pen the user manual included in the package leaflet must be read carefully. The pre-filled pen has to be used as recommended in the user manual.

Pens should not be used if any part looks broken or damaged.

Injecting a dose

If using a pre-filled or reusable pen refer to the detailed instructions for preparing the pen and injecting the dose, the following is a general description.

1. Wash your hands
2. Choose a site for injection.
3. Clean the skin as instructed.
4. Stabilise the skin by spreading it or pinching up a large area. Insert the needle and inject as instructed.
5. Pull the needle out and apply gentle pressure over the injection site for several seconds. Do not rub the area.
6. Dispose of the syringe and needle safely. For an injection device use the outer needle cap, unscrew the needle and dispose of it safely.
7. Use of the injection sites should be rotated so that the same is not used more than approximately once a month.

Humalog Tempo Pen

The Tempo Pen is designed to work with the Tempo Smart Button. The Tempo Smart Button is an optional product that can be attached to the Tempo Pen dose knob and aids in transmitting Humalog dose information from the Tempo Pen to a compatible mobile application. The Tempo Pen injects insulin with or without the Tempo Smart Button attached. To transmit data to the mobile application, follow the instructions provided with the Tempo Smart Button and the instructions with the mobile application

Any unused product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Eli Lilly Nederland B.V., Orteliuslaan 1000, 3528 BD Utrecht, The Netherlands.

8. MARKETING AUTHORISATION NUMBERS

EU/1/96/007/002
EU/1/96/007/004
EU/1/96/007/020
EU/1/96/007/021
EU/1/96/007/023
EU/1/96/007/031
EU/1/96/007/032
EU/1/96/007/043
EU/1/96/007/044
EU/1/96/007/045
EU/1/96/007/046
EU/1/96/007/047

9. DATE OF FIRST AUTHORISATION/RENEWAL OF AUTHORISATION

Date of first authorisation: 30th April 1996
Date of last renewal: 30th April 2006

10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency https://www.ema.europa.eu

1. NAME OF THE MEDICINAL PRODUCT

Humalog Mix25 100 units/ml suspension for injection in vial
Humalog Mix25 100 units/ml suspension for injection in cartridge
Humalog Mix25 100 units/ml KwikPen suspension for injection in a pre-filled pen

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains 100 units insulin lispro* (equivalent to 3.5mg).

Humalog Mix25 consists of 25% insulin lispro solution and 75% insulin lispro protamine suspension.

Vial

Each vial contains 1000 units of insulin lispro in 10 ml suspension.

Cartridge

Each cartridge contains 300 units of insulin lispro in 3 ml suspension.

KwikPen

Each pre-filled pen contains 300 units of insulin lispro in 3 ml suspension.
Each KwikPen delivers 1-60 units in steps of 1 unit.

*produced in *E.coli* by recombinant DNA technology.

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Suspension for injection.

White suspension.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Humalog Mix25 is indicated for the treatment of patients with diabetes mellitus who require insulin for the maintenance of normal glucose homeostasis.

4.2 Posology and method of administration

Posology

The dosage should be determined by the physician, according to the requirement of the patient.

Humalog Mix25 may be given shortly before meals. When necessary, Humalog Mix25 can be given soon after meals. Humalog Mix25 should only be given by subcutaneous injection. Under no circumstances should Humalog Mix25 be given intravenously.

The rapid onset and early peak of activity of Humalog itself is observed following the subcutaneous administration of Humalog Mix25. This allows Humalog Mix25 to be given very close to mealtime.

The duration of action of the insulin lispro protamine suspension component of Humalog Mix25 is similar to that of a basal insulin (NPH).

The time course of action of any insulin may vary considerably in different individuals or at different times in the same individual. As with all insulin preparations, the duration of action of Humalog Mix25 is dependent on dose, site of injection, blood supply, temperature, and physical activity.

Special populations

Renal impairment
Insulin requirements may be reduced in the presence of renal impairment.

Hepatic impairment
Insulin requirements may be reduced in patients with hepatic impairment due to reduced capacity for gluconeogenesis and reduced insulin breakdown; however, in patients with chronic hepatic impairment, an increase in insulin resistance may lead to increased insulin requirements.

Paediatric population
Administration of Humalog Mix25 to children below 12 years of age should be considered only in case of an expected benefit when compared to soluble insulin.

Method of administration

Subcutaneous administration should be in the upper arms, thighs, buttocks, or abdomen. Use of injection sites should be rotated so that the same site is not used more than approximately once a month, in order to reduce the risk of lipodystrophy and cutaneous amyloidosis (see section 4.4 and 4.8).

When administered subcutaneously care should be taken when injecting Humalog Mix25 to ensure that a blood vessel has not been entered. After injection, the site of injection should not be massaged. Patients must be educated to use the proper injection techniques.

KwikPen

The KwikPen delivers 1 – 60 units in steps of 1 unit in a single injection. The needed dose is dialled in units. **The number of units is shown in the dose window of the pen**.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

Hypoglycaemia.

4.4 Special warnings and precautions for use

Traceability

In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.

Under no circumstances should Humalog Mix25 be given intravenously.

Transferring a patient to another type or brand of insulin

Transferring a patient to another type or brand of insulin should be done under strict medical supervision. Changes in strength, brand (manufacturer), type (regular/soluble, NPH/isophane, etc.),

species (animal, human, human insulin analogue), and/or method of manufacture (recombinant DNA versus animal-source insulin) may result in the need for a change in dosage.

Hypoglycaemia and hyperglycaemia

Conditions which may make the early warning symptoms of hypoglycaemia different or less pronounced include long duration of diabetes, intensified insulin therapy, diabetic nerve disease or medications such as beta-blockers.

A few patients who have experienced hypoglycaemic reactions after transfer from animal-source insulin to human insulin have reported that the early warning symptoms of hypoglycaemia were less pronounced or different from those experienced with their previous insulin. Uncorrected hypoglycaemic or hyperglycaemic reactions can cause loss of consciousness, coma, or death.

The use of dosages which are inadequate or discontinuation of treatment, especially in insulin-dependent diabetics, may lead to hyperglycaemia and diabetic ketoacidosis; conditions which are potentially lethal.

Injection technique

Patients must be instructed to perform continuous rotation of the injection site to reduce the risk of developing lipodystrophy and cutaneous amyloidosis. There is a potential risk of delayed insulin absorption and worsened glycaemic control following insulin injections at sites with these reactions. A sudden change in the injection site to an unaffected area has been reported to result in hypoglycaemia. Blood glucose monitoring is recommended after the change in the injection site, and dose adjustment of antidiabetic medications may be considered.

Insulin requirements and dosage adjustment

Insulin requirements may be increased during illness or emotional disturbances.

Adjustment of dosage may also be necessary if patients undertake increased physical activity or change their usual diet. Exercise taken immediately after a meal may increase the risk of hypoglycaemia.

Combination of Humalog Mix25 with pioglitazone

Cases of cardiac failure have been reported when pioglitazone was used in combination with insulin, especially in patients with risk factors for development of cardiac heart failure. This should be kept in mind, if treatment with the combination of pioglitazone and Humalog Mix25 is considered. If the combination is used, patients should be observed for signs and symptoms of heart failure, weight gain and oedema. Pioglitazone should be discontinued, if any deterioration in cardiac symptoms occurs.

Avoidance of medication errors

Patients must be instructed to always check the insulin label before each injection to avoid accidental mix-ups between the two different strengths of Humalog KwikPen as well as other insulin products. Patients must visually verify the dialled units on the dose counter of the pen. Therefore, the requirement for patients to self-inject is that they can read the dose counter on the pen. Patients who are blind or have poor vision must be instructed to always get help/assistance from another person who has good vision and is trained in using the insulin device.

Excipients

This medicinal product contains less than 1 mmol sodium (23 mg) per dose, i.e., essentially “sodium-free”.

4.5 Interaction with other medicinal products and other forms of interaction

Insulin requirements may be increased by substances with hyperglycaemic activity, such as oral contraceptives, corticosteroids, or thyroid replacement therapy, danazol, $beta_2$ stimulants (such as ritodrine, salbutamol, terbutaline).

Insulin requirements may be reduced in the presence of substances with hypoglycaemic activity, such as oral hypoglycaemics, salicylates (for example, acetylsalicylic acid), sulphate antibiotics, certain antidepressants (monoamine oxidase inhibitors, selective serotonin reuptake inhibitors), certain angiotensin converting enzyme inhibitors (captopril, enalapril), angiotensin II receptor blockers, beta-blockers, octreotide or alcohol.

Mixing Humalog Mix25 with other insulins has not been studied.

The physician should be consulted when using other medications in addition to Humalog Mix25 (see section 4.4).

4.6 Fertility, pregnancy and lactation

Pregnancy

Data on a large number of exposed pregnancies do not indicate any adverse effect of insulin lispro on pregnancy or on the health of the foetus/newborn.

It is essential to maintain good control of the insulin-treated (insulin-dependent or gestational diabetes) patient throughout pregnancy. Insulin requirements usually fall during the first trimester and increase during the second and third trimesters. Patients with diabetes should be advised to inform their doctor if they are pregnant or are contemplating pregnancy. Careful monitoring of glucose control, as well as general health, is essential in pregnant patients with diabetes.

Breast-feeding

Patients with diabetes who are breast-feeding may require adjustments in insulin dose, diet or both.

Fertility

Insulin lispro did not induce fertility impairment in animal studies (see section 5.3).

4.7 Effects on ability to drive and use machines

The patient’s ability to concentrate and react may be impaired as a result of hypoglycaemia. This may constitute a risk in situations where these abilities are of special importance (e.g. driving a car or operating machinery).

Patients should be advised to take precautions to avoid hypoglycaemia whilst driving, this is particularly important in those who have reduced or absent awareness of the warning signs of hypoglycaemia or have frequent episodes of hypoglycaemia. The advisability of driving should be considered in these circumstances.

4.8 Undesirable effects

Summary of safety profile

Hypoglycaemia is the most frequent undesirable effect of insulin therapy that a patient with diabetes may suffer. Severe hypoglycaemia may lead to loss of consciousness, and in extreme cases, death. No specific frequency for hypoglycaemia is presented, since hypoglycaemia is a result of both the insulin dose and other factors e.g. a patient`s level of diet and exercise.

Tabulated list of adverse reactions

The following related adverse reactions from clinical trials are listed below as MedDRA preferred term by system organ class and in order of decreasing incidence (very common: ≥1/10; common: ≥1/100 to <1/10; uncommon: ≥1/1,000 to <1/100; rare: ≥1/10,000 to <1/1,000; very rare: <1/10,000) ; not known (cannot be estimated form the available data).

Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.

MedDRA system organ classes	**Very common**	**Common**	**Uncommon**	**Rare**	**Very rare**	**Not known**
Immune system disorders						
Local allergy		X				
Systemic allergy				X		
Skin and subcutaneous tissue disorders						
Lipodystrophy			X			
Cutaneous amyloidosis						X

Description of selected adverse reactions

Local allergy

Local allergy in patients is common . Redness, swelling, and itching can occur at the site of insulin injection. This condition usually resolves in a few days to a few weeks. In some instances, this condition may be related to factors other than insulin, such as irritants in the skin cleansing agent or poor injection technique.

Systemic allergy

Systemic allergy, which is rare but potentially more serious, is a generalised allergy to insulin. It may cause a rash over the whole body, shortness of breath, wheezing, reduction in blood pressure, fast pulse, or sweating. Severe cases of generalised allergy may be life-threatening.

Skin and subcutaneous tissue disorders

Lipodystrophy and cutaneous amyloidosis may occur at the injection site and delay local insulin absorption. Continuous rotation of the injection site within the given injection area may help to reduce or prevent these reactions (see section 4.4).

Oedema

Cases of oedema have been reported with insulin therapy, particularly if previous poor metabolic control is improved by intensified insulin therapy.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V.

4.9 Overdose

Insulins have no specific overdose definitions because serum glucose concentrations are a result of complex interactions between insulin levels, glucose availability and other metabolic processes. Hypoglycaemia may occur as a result of an excess of insulin activity relative to food intake and energy expenditure.

Hypoglycaemia may be associated with listlessness, confusion, palpitations, headache, sweating and vomiting.

Mild hypoglycaemic episodes will respond to oral administration of glucose or other sugar or saccharated products.

Correction of moderately severe hypoglycaemia can be accomplished by intramuscular or subcutaneous administration of glucagon, followed by oral carbohydrate when the patient recovers sufficiently. Patients who fail to respond to glucagon must be given glucose solution intravenously.

If the patient is comatose, glucagon should be administered intramuscularly or subcutaneously. However, glucose solution must be given intravenously if glucagon is not available or if the patient fails to respond to glucagon. The patient should be given a meal as soon as consciousness is recovered.

Sustained carbohydrate intake and observation may be necessary because hypoglycaemia may recur after apparent clinical recovery.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Drugs used in diabetes, insulins and analogues for injection, intermediate or long acting combined with fast acting. ATC Code: A10A D04.

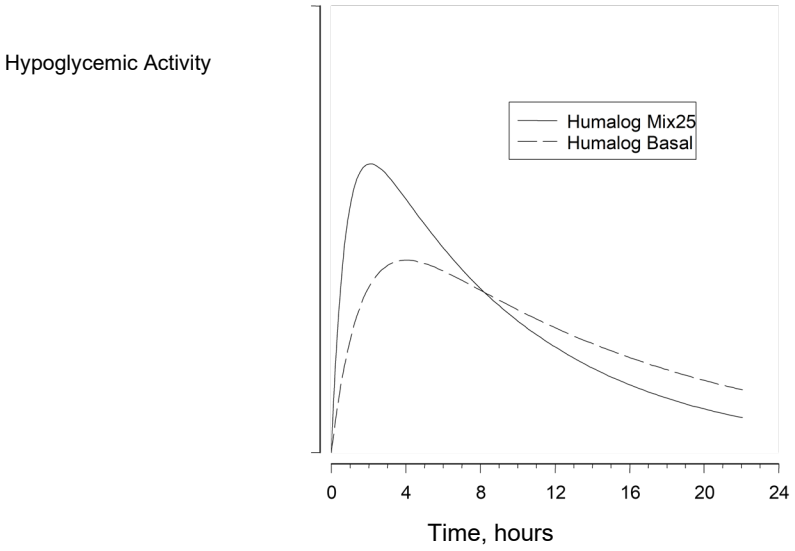
The primary activity of insulin lispro is the regulation of glucose metabolism.

In addition, insulins have several anabolic and anti-catabolic actions on a variety of different tissues. Within muscle tissue this includes increasing glycogen, fatty acid, glycerol and protein synthesis and amino acid uptake, while decreasing glycogenolysis, gluconeogenesis, ketogenesis, lipolysis, protein catabolism and amino acid output.

Insulin lispro has a rapid onset of action (approximately 15 minutes), thus allowing it to be given closer to a meal (within zero to 15 minutes of the meal) when compared to soluble insulin (30 to 45 minutes before). The rapid onset and early peak of activity of insulin lispro is observed following the subcutaneous administration of Humalog Mix25. Humalog BASAL has an activity profile that is very similar to that of a basal insulin (NPH) over a period of approximately 15 hours.

Clinical trials in patients with type 1 and type 2 diabetes have demonstrated reduced postprandial hyperglycaemia with Humalog Mix25 compared to human insulin mixture 30/70. In one clinical study there was a small (0.38 mmol/l) increase in blood glucose levels at night (3a.m.).

In the figure below the pharmacodynamics of Humalog Mix25 and BASAL are illustrated.



The above representation reflects the relative amount of glucose over time required to maintain the subject's whole blood glucose concentrations near fasting levels and is an indicator of the effect of these insulins on glucose metabolism over time.

The glucodynamic response to insulin lispro is not affected by renal or hepatic function impairment. Glucodynamic differences between insulin lispro and soluble human insulin, as measured during a glucose clamp procedure, were maintained over a wide range of renal function.

Insulin lispro has been shown to be equipotent to human insulin on a molar basis but its effect is more rapid and of a shorter duration.

In two 8-month open label crossover studies, type 2 diabetes patients who were either new to insulin therapy or already using one or two injections of insulin, received 4 months of treatment with Humalog Mix25 (used twice daily with metformin) and insulin glargine (used once daily with metformin) in a randomised sequence. Detailed information can be found in the following table.

	Insulin-Naive Patients n = 78	**Not Insulin-Naive Patients** n = 97
Mean total daily insulin dose at endpoint	0.63 units/kg	0.42 units/kg
Haemoglobin A1c –Reduction[1]	1.30% (mean at baseline = 8.7%)	1.00 % (mean at baseline = 8.5%)
Reduction of the mean of combined morning / evening two-hour postprandial blood glucose[1]	3.46 mM	2.48 mM
Reduction of the mean fasting blood glucose[1]	0.55 mM	0.65 mM
Incidence of hypoglycaemia at endpoint	25%	25%
Bodyweight gain[2]	2.33 kg	0.96 kg

1 from baseline to end of Humalog Mix25 treatment

2 in patients randomised to Humalog Mix25 during the first crossover period

5.2 Pharmacokinetic properties

The pharmacokinetics of insulin lispro reflect a compound that is rapidly absorbed, and achieves peak blood levels 30 to 70 minutes following subcutaneous injection. The pharmacokinetics of insulin lispro protamine suspension are consistent with those of an intermediate acting insulin such as NPH. The pharmacokinetics of Humalog Mix25 are representative of the individual pharmacokinetic properties of the two components. When considering the clinical relevance of these kinetics, it is more appropriate to examine the glucose utilisation curves (as discussed in 5.1).

Insulin lispro maintains more rapid absorption when compared to soluble human insulin in patients with renal impairment. In patients with type 2 diabetes over a wide range of renal function the pharmacokinetic differences between insulin lispro and soluble human insulin were generally maintained and shown to be independent of renal function. Insulin lispro maintains more rapid absorption and elimination when compared to soluble human insulin in patients with hepatic impairment.

5.3 Preclinical safety data

In *in vitro* tests, including binding to insulin receptor sites and effects on growing cells, insulin lispro behaved in a manner that closely resembled human insulin. Studies also demonstrate that the dissociation of binding to the insulin receptor of insulin lispro is equivalent to human insulin. Acute, one month and twelve month toxicology studies produced no significant toxicity findings.

Insulin lispro did not induce fertility impairment, embryotoxicity or teratogenicity in animal studies.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Protamine sulphate
m-Cresol
Phenol
Glycerol
Dibasic sodium phosphate.$7H_2O$
Zinc oxide
Water for injections
Hydrochloric acid and sodium hydroxide may be used to adjust pH.

6.2 Incompatibilities

Mixing Humalog Mix25 with other insulins has not been studied. In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 Shelf life

Before use

3 years.

After first use /after cartridge insertion

28 days.

6.4 Special precautions for storage

Do not freeze. Do not expose to excessive heat or direct sunlight.

Before use

Store in a refrigerator (2°C - 8°C).

After first use /after cartridge insertion

Vial

Store in a refrigerator (2°C - 8°C) or below 30°C.

Cartridge

Store below 30°C. Do not refrigerate. The pen with the inserted cartridge should not be stored with the needle attached.

KwikPen

Store below 30°C. Do not refrigerate. The pre-filled pen should not be stored with the needle attached.

6.5 Nature and contents of container

Vial

The suspension is contained in type I flint glass vials, sealed with butyl or halobutyl stoppers and secured with aluminium seals. Dimeticone or silicone emulsion may have been used to treat the vial stoppers.

10 ml Vial: Pack of 1 vial. Not all packs may be marketed.

Cartridge

The suspension is contained in type I flint glass cartridges, sealed with butyl or halobutyl disc seals and plunger heads and secured with aluminium seals. Dimeticone or silicone emulsion may have been used to treat the cartridge plunger, and/or the glass cartridge.

3 ml Cartridge: Packs of 5 or 10 cartridges. Not all packs may be marketed.

KwikPen

The suspension is contained in type I flint glass cartridges, sealed with halobutyl disc seals and plunger heads and secured with aluminium seals. Dimeticone or silicone emulsion may have been used to treat the cartridge plunger, and/or the glass cartridge. The 3 ml cartridges are sealed in a disposable pen injector, called the "KwikPen". Needles are not included.

3 ml KwikPen: Packs of 5 pre-filled pens or a multipack of 10 (2 packs of 5) pre-filled pens. Not all packs may be marketed.

6.6 Special precautions for disposal and other handling

Instructions for use and handling

To prevent the possible transmission of disease, each cartridge or pen must be used by one patient only, even if the needle on the delivery device is changed. Patients using vials must never share needles or syringes. The patient should discard the needle after every injection.

The Humalog Mix25 should be examined frequently and should not be used if clumps of material are present or if solid white particles stick to the bottom or wall of the container, giving it a frosted appearance.

Preparing a dose

Vials containing Humalog Mix25 should be rotated in the palms of the hands before use to resuspend the insulin until it appears uniformly cloudy or milky. Cartridges and KwikPens containing Humalog Mix25 should be rotated in the palms of the hands ten times and inverted 180° ten times immediately before use to resuspend the insulin until it appears uniformly cloudy or milky.

If not, repeat the above procedure until contents are mixed. Cartridges contain a small glass bead to assist mixing.

Do not shake vigorously as this may cause frothing which may interfere with the correct measurement of the dose.

Vial
The vial is to be used in conjunction with an appropriate syringe (100 unit markings).

1. Wash your hands.

2. If using a new vial, flip off the plastic protective cap, but **do not** remove the stopper.

3. Draw air into the syringe equal to the prescribed Humalog Mix25 dose. Wipe the top of the vial with a swab. Put the needle through rubber top of the Humalog Mix25 vial and inject the air into the vial.

4. Turn the vial and syringe upside down. Hold the vial and syringe firmly in one hand.

5. Making sure the tip of the needle is in the Humalog Mix25, withdraw the correct dose into the syringe.

6. Before removing the needle from the vial, check the syringe for air bubbles that reduce the amount of Humalog Mix25 in it. If bubbles are present, hold the syringe straight up and tap its side until the bubbles float to the top. Push them out with the plunger and withdraw the correct dose.

7. Remove the needle from the vial and lay the syringe down so that the needle does not touch anything.

Cartridge
Humalog Mix25 cartridges are to be used with a Lilly reusable insulin pen and should not be used with any other reusable pen as the dosing accuracy has not been established with other pens.

The instructions with each individual pen must be followed for loading the cartridge, attaching the needle and administering the insulin injection.

KwikPen
Before using the KwikPen the user manual included in the package leaflet must be read carefully. The KwikPen has to be used as recommended in the user manual.

Pens should not be used if any part looks broken or damaged.

Injecting a dose

If using a pre-filled or reusable pen refer to the detailed instructions for preparing the pen and injecting the dose, the following is a general description.

1. Wash your hands

2. Choose a site for injection.

3. Clean the skin as instructed.

4. Stabilise the skin by spreading it or pinching up a large area. Insert the needle and inject as instructed.

5. Pull the needle out and apply gentle pressure over the injection site for several seconds. Do not rub the area.

6. Dispose of the syringe and needle safely. For an injection device use the outer needle cap, unscrew the needle and dispose of it safely.

7. Use of the injection sites should be rotated so that the same is not used more than approximately once a month.

Any unused product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Eli Lilly Nederland B.V., Orteliuslaan 1000, 3528 BD Utrecht, The Netherlands.

8. MARKETING AUTHORISATION NUMBERS

EU/1/96/007/005
EU/1/96/007/008
EU/1/96/007/024
EU/1/96/007/033
EU/1/96/007/034

9. DATE OF FIRST AUTHORISATION/RENEWAL OF AUTHORISATION

Date of first authorisation: 30th April 1996
Date of last renewal: 30th April 2006

10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency https://www.ema.europa.eu

1. NAME OF THE MEDICINAL PRODUCT

Humalog Mix50 100 units/ml suspension for injection in cartridge
Humalog Mix50 100 units/ml KwikPen suspension for injection in a pre-filled pen

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains 100 units insulin lispro* (equivalent to 3.5mg).

Humalog Mix50 consists of 50% insulin lispro solution and 50% insulin lispro protamine suspension.

Cartridge

Each cartridge contains 300 units of insulin lispro in 3 ml suspension.

KwikPen

Each pre-filled pen contains 300 units of insulin lispro in 3 ml suspension.
Each KwikPen delivers 1-60 units in steps of 1 unit.

*produced in *E.coli* by recombinant DNA technology.

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Suspension for injection.

White suspension.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Humalog Mix50 is indicated for the treatment of patients with diabetes mellitus who require insulin for the maintenance of normal glucose homeostasis.

4.2 Posology and method of administration

Posology

The dosage should be determined by the physician, according to the requirement of the patient.

Humalog Mix50 may be given shortly before meals. When necessary, Humalog Mix50 can be given soon after meals. Humalog Mix50 should only be given by subcutaneous injection. Under no circumstances should Humalog Mix50 be given intravenously.

The rapid onset and early peak of activity of Humalog itself is observed following the subcutaneous administration of Humalog Mix50. This allows Humalog Mix50 to be given very close to mealtime. The duration of action of the insulin lispro protamine suspension component of Humalog Mix50 is similar to that of a basal insulin (NPH).

The time course of action of any insulin may vary considerably in different individuals or at different times in the same individual. As with all insulin preparations, the duration of action of Humalog Mix50 is dependent on dose, site of injection, blood supply, temperature, and physical activity.

Special populations

Renal impairment
Insulin requirements may be reduced in the presence of renal impairment.

Hepatic impairment
Insulin requirements may be reduced in patients with hepatic impairment due to reduced capacity for gluconeogenesis and reduced insulin breakdown; however, in patients with chronic hepatic impairment, an increase in insulin resistance may lead to increased insulin requirements.

Paediatric population
Administration of Humalog Mix50 to children below 12 years of age should be considered only in case of an expected benefit when compared to soluble insulin.

Method of administration

Subcutaneous administration should be in the upper arms, thighs, buttocks, or abdomen. Use of injection sites should be rotated so that the same site is not used more than approximately once a month, in order to reduce the risk of lipodystrophy and cutaneous amyloidosis (see section 4.4 and 4.8).

When administered subcutaneously care should be taken when injecting Humalog Mix50 to ensure that a blood vessel has not been entered. After injection, the site of injection should not be massaged. Patients must be educated to use the proper injection techniques.

KwikPen

The KwikPen delivers 1 – 60 units in steps of 1 unit in a single injection. The needed dose is dialled in units. **The number of units is shown in the dose window of the pen**.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

Hypoglycaemia.

4.4 Special warnings and precautions for use

Traceability

In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.

Under no circumstances should Humalog Mix50 be given intravenously.

Transferring a patient to another type or brand of insulin

Transferring a patient to another type or brand of insulin should be done under strict medical supervision. Changes in strength, brand (manufacturer), type (regular/soluble, NPH/isophane, etc.), species (animal, human, human insulin analogue), and/or method of manufacture (recombinant DNA versus animal-source insulin) may result in the need for a change in dosage.

Hypoglycaemia and hyperglycaemia

Conditions which may make the early warning symptoms of hypoglycaemia different or less pronounced include long duration of diabetes, intensified insulin therapy, diabetic nerve disease or medications such as beta-blockers.

A few patients who have experienced hypoglycaemic reactions after transfer from animal-source insulin to human insulin have reported that the early warning symptoms of hypoglycaemia were less pronounced or different from those experienced with their previous insulin. Uncorrected hypoglycaemic or hyperglycaemic reactions can cause loss of consciousness, coma, or death.

The use of dosages which are inadequate or discontinuation of treatment, especially in insulin-dependent diabetics, may lead to hyperglycaemia and diabetic ketoacidosis; conditions which are potentially lethal.

Injection technique

Patients must be instructed to perform continuous rotation of the injection site to reduce the risk of developing lipodystrophy and cutaneous amyloidosis. There is a potential risk of delayed insulin absorption and worsened glycaemic control following insulin injections at sites with these reactions. A sudden change in the injection site to an unaffected area has been reported to result in hypoglycaemia. Blood glucose monitoring is recommended after the change in the injection site, and dose adjustment of antidiabetic medications may be considered.

Insulin requirements and dosage adjustment

Insulin requirements may be increased during illness or emotional disturbances.

Adjustment of dosage may also be necessary if patients undertake increased physical activity or change their usual diet. Exercise taken immediately after a meal may increase the risk of hypoglycaemia.

Combination of Humalog Mix50 with pioglitazone

Cases of cardiac failure have been reported when pioglitazone was used in combination with insulin, especially in patients with risk factors for development of cardiac heart failure. This should be kept in mind, if treatment with the combination of pioglitazone and Humalog Mix50 is considered. If the combination is used, patients should be observed for signs and symptoms of heart failure, weight gain and oedema. Pioglitazone should be discontinued, if any deterioration in cardiac symptoms occurs.

Avoidance of medication errors

Patients must be instructed to always check the insulin label before each injection to avoid accidental mix-ups between the two different strengths of Humalog KwikPen as well as other insulin products. Patients must visually verify the dialled units on the dose counter of the pen. Therefore, the requirement for patients to self-inject is that they can read the dose counter on the pen. Patients who are blind or have poor vision must be instructed to always get help/assistance from another person who has good vision and is trained in using the insulin device.

Excipients

This medicinal product contains less than 1 mmol sodium (23 mg) per dose, i.e., essentially “sodium-free”.

4.5 Interaction with other medicinal products and other forms of interaction

Insulin requirements may be increased by substances with hyperglycaemic activity, such as oral contraceptives, corticosteroids, or thyroid replacement therapy, danazol, beta$_2$ stimulants (such as ritodrine, salbutamol, terbutaline).

Insulin requirements may be reduced in the presence of substances with hypoglycaemic activity, such as oral hypoglycaemics, salicylates (for example, acetylsalicylic acid), sulpha antibiotics, certain antidepressants, (monoamine oxidase inhibitors, selective serotonin reuptake inhibitors), certain angiotensin converting enzyme inhibitors (captopril, enalapril), angiotensin II receptor blockers, beta-blockers, octreotide or alcohol.

Mixing Humalog Mix50 with other insulins has not been studied.

The physician should be consulted when using other medications in addition to Humalog Mix50 (see section 4.4).

4.6 Fertility, pregnancy and lactation

Pregnancy

Data on a large number of exposed pregnancies do not indicate any adverse effect of insulin lispro on pregnancy or on the health of the foetus/newborn.

It is essential to maintain good control of the insulin-treated (insulin-dependent or gestational diabetes) patient throughout pregnancy. Insulin requirements usually fall during the first trimester and increase during the second and third trimesters. Patients with diabetes should be advised to inform their doctor if they are pregnant or are contemplating pregnancy. Careful monitoring of glucose control, as well as general health, is essential in pregnant patients with diabetes.

Breast-feeding

Patients with diabetes who are breast-feeding may require adjustments in insulin dose, diet or both.

Fertility

Insulin lispro did not induce fertility impairment in animal studies (see section 5.3).

4.7 Effects on ability to drive and use machines

The patient’s ability to concentrate and react may be impaired as a result of hypoglycaemia. This may constitute a risk in situations where these abilities are of special importance (e.g. driving a car or operating machinery).

Patients should be advised to take precautions to avoid hypoglycaemia whilst driving, this is particularly important in those who have reduced or absent awareness of the warning signs of hypoglycaemia or have frequent episodes of hypoglycaemia. The advisability of driving should be considered in these circumstances.

4.8 Undesirable effects

Summary of safety profile

Hypoglycaemia is the most frequent undesirable effect of insulin therapy that a patient with diabetes may suffer. Severe hypoglycaemia may lead to loss of consciousness, and in extreme cases, death. No specific frequency for hypoglycaemia is presented, since hypoglycaemia is a result of both the insulin dose and other factors e.g. a patient`s level of diet and exercise.

Tabulated list of adverse reactions

The following related adverse reactions from clinical trials are listed below as MedDRA preferred term by system organ class and in order of decreasing incidence (very common: ≥1/10; common: ≥1/100 to <1/10; uncommon: ≥1/1,000 to <1/100; rare: ≥1/10,000 to <1/1,000; very rare: <1/10,000) ; not known (cannot be estimated form the available data).

Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.

MedDRA system organ classes	**Very common**	**Common**	**Uncommon**	**Rare**	**Very rare**	**Not known**
Immune system disorders						
Local allergy		X				
Systemic allergy				X		
Skin and subcutaneous tissue disorders						
Lipodystrophy			X			
Cutaneous amyloidosis						X

Description of selected adverse reactions

Local allergy

Local allergy in patients is common . Redness, swelling, and itching can occur at the site of insulin injection. This condition usually resolves in a few days to a few weeks. In some instances, this condition may be related to factors other than insulin, such as irritants in the skin cleansing agent or poor injection technique.

Systemic allergy

Systemic allergy, which is rare but potentially more serious, is a generalised allergy to insulin. It may cause a rash over the whole body, shortness of breath, wheezing, reduction in blood pressure, fast pulse, or sweating. Severe cases of generalised allergy may be life-threatening.

Skin and subcutaneous tissue disorders

Lipodystrophy and cutaneous amyloidosis may occur at the injection site and delay local insulin absorption. Continuous rotation of the injection site within the given injection area may help to reduce or prevent these reactions (see section 4.4).

Oedema

Cases of oedema have been reported with insulin therapy, particularly if previous poor metabolic control is improved by intensified insulin therapy.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V.

4.9 Overdose

Insulins have no specific overdose definitions because serum glucose concentrations are a result of complex interactions between insulin levels, glucose availability and other metabolic processes. Hypoglycaemia may occur as a result of an excess of insulin activity relative to food intake and energy expenditure.

Hypoglycaemia may be associated with listlessness, confusion, palpitations, headache, sweating and vomiting.

Mild hypoglycaemic episodes will respond to oral administration of glucose or other sugar or saccharated products.

Correction of moderately severe hypoglycaemia can be accomplished by intramuscular or subcutaneous administration of glucagon, followed by oral carbohydrate when the patient recovers sufficiently. Patients who fail to respond to glucagon must be given glucose solution intravenously.

If the patient is comatose, glucagon should be administered intramuscularly or subcutaneously. However, glucose solution must be given intravenously if glucagon is not available or if the patient fails to respond to glucagon. The patient should be given a meal as soon as consciousness is recovered.

Sustained carbohydrate intake and observation may be necessary because hypoglycaemia may recur after apparent clinical recovery.

5. PHARMACOLOGICAL PROPERTIES

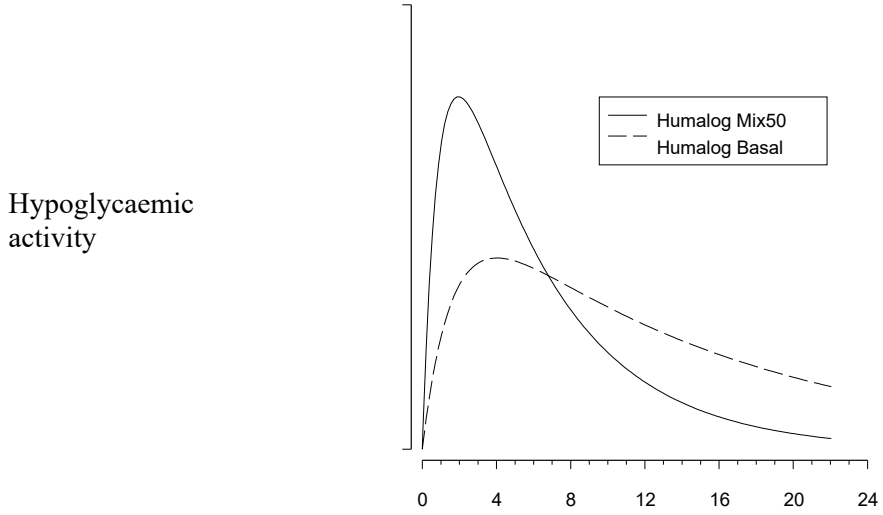
5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Drugs used in diabetes, insulins and analogues for injection, intermediate or long acting combined with fast acting. ATC Code: A10A D04.

The primary activity of insulin lispro is the regulation of glucose metabolism.

In addition, insulins have several anabolic and anti-catabolic actions on a variety of different tissues. Within muscle tissue this includes increasing glycogen, fatty acid, glycerol and protein synthesis and amino acid uptake, while decreasing glycogenolysis, gluconeogenesis, ketogenesis, lipolysis, protein catabolism and amino acid output.

Insulin lispro has a rapid onset of action (approximately 15 minutes), thus allowing it to be given closer to a meal (within zero to 15 minutes of the meal) when compared to soluble insulin (30 to 45 minutes before). The rapid onset and early peak of activity of insulin lispro is observed following the subcutaneous administration of Humalog Mix50. Humalog BASAL has an activity profile that is very similar to that of a basal insulin (NPH) over a period of approximately 15 hours. In the figure below the pharmacodynamics of Humalog Mix50 and BASAL are illustrated.



The above representation reflects the relative amount of glucose over time required to maintain the subject's whole blood glucose concentrations near fasting levels and is an indicator of the effect of these insulins on glucose metabolism over time.

The glucodynamic response to insulin lispro is not affected by renal or hepatic function impairment. Glucodynamic differences between insulin lispro and soluble human insulin, as measured during a glucose clamp procedure, were maintained over a wide range of renal function.

Insulin lispro has been shown to be equipotent to human insulin on a molar basis but its effect is more rapid and of a shorter duration.

5.2 Pharmacokinetic properties

The pharmacokinetics of insulin lispro reflect a compound that is rapidly absorbed, and achieves peak blood levels 30 to 70 minutes following subcutaneous injection. The pharmacokinetics of insulin lispro protamine suspension are consistent with those of an intermediate acting insulin such as NPH. The pharmacokinetics of Humalog Mix50 are representative of the individual pharmacokinetic properties of the two components. When considering the clinical relevance of these kinetics, it is more appropriate to examine the glucose utilisation curves (as discussed in 5.1).

Insulin lispro maintains more rapid absorption when compared to soluble human insulin in patients with renal impairment. In patients with type 2 diabetes over a wide range of renal function the pharmacokinetic differences between insulin lispro and soluble human insulin were generally maintained and shown to be independent of renal function. Insulin lispro maintains more rapid absorption and elimination when compared to soluble human insulin in patients with hepatic impairment.

5.3 Preclinical safety data

In *in vitro* tests, including binding to insulin receptor sites and effects on growing cells, insulin lispro behaved in a manner that closely resembled human insulin. Studies also demonstrate that the

dissociation of binding to the insulin receptor of insulin lispro is equivalent to human insulin. Acute, one month and twelve month toxicology studies produced no significant toxicity findings.

Insulin lispro did not induce fertility impairment, embryotoxicity or teratogenicity in animal studies.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Protamine sulphate
m-Cresol
Phenol
Glycerol
Dibasic sodium phosphate.$7H_2O$
Zinc oxide
Water for injections
Hydrochloric acid and sodium hydroxide may be used to adjust pH.

6.2 Incompatibilities

Mixing Humalog Mix50 with other insulins has not been studied. In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 Shelf life

Before use

3 years.

After first use/ after cartridge insertion

28 days.

6.4 Special precautions for storage

Do not freeze. Do not expose to excessive heat or direct sunlight.

Before use

Store in a refrigerator (2°C - 8°C).

After first use/ after cartridge insertion

Cartridge

Store below 30°C. Do not refrigerate. The pen with the inserted cartridge should not be stored with the needle attached.

KwikPen

Store below 30°C. Do not refrigerate. The pre-filled pen should not be stored with the needle attached.

6.5 Nature and contents of container

Cartridge

The suspension is contained in type I flint glass cartridges, sealed with butyl or halobutyl disc seals and plunger heads and secured with aluminium seals. Dimeticone or silicone emulsion may have been used to treat the cartridge plunger, and/or the glass cartridge.

3 ml Cartridge: Packs of 5 or 10. Not all packs may be marketed.

KwikPen

The suspension is contained in type I flint glass cartridges, sealed with halobutyl disc seals and plunger heads and secured with aluminium seals. Dimeticone or silicone emulsion may have been used to treat the cartridge plunger, and/or the glass cartridge. The 3 ml cartridges are sealed in a disposable pen injector, called the "KwikPen". Needles are not included.
3 ml KwikPen: Packs of 5 or a multipack of 10 (2 packs of 5). Not all packs may be marketed.

6.6 Special precautions for disposal and other handling

Instructions for use and handling

To prevent the possible transmission of disease, each cartridge or pen must be used by one patient only, even if the needle on the delivery device is changed. The patient should discard the needle after every injection.

The Humalog Mix50 should be examined frequently and should not be used if clumps of material are present or if solid white particles stick to the bottom or wall of the container, giving it a frosted appearance.

Preparing a dose

Cartridges or KwikPens containing Humalog Mix50 should be rotated in the palms of the hands ten times and inverted 180° ten times immediately before use to resuspend the insulin until it appears uniformly cloudy or milky. If not, repeat the above procedure until contents are mixed. Cartridges contain a small glass bead to assist mixing.

Do not shake vigorously as this may cause frothing which may interfere with the correct measurement of the dose.

Cartridge
Humalog Mix50 cartridges are to be used with a Lilly reusable insulin pen and should not be used with any other reusable pen as the dosing accuracy has not been established with other pens.

The instructions with each individual pen must be followed for loading the cartridge, attaching the needle and administering the insulin injection.

KwikPen
Before using the KwikPen the user manual included in the package leaflet must be read carefully. The KwikPen has to be used as recommended in the user manual.

Pens should not be used if any part looks broken or damaged.

Injecting a dose

If using a pre-filled or reusable pen refer to the detailed instructions for preparing the pen and injecting the dose, the following is a general description.

1. Wash your hands.

2. Choose a site for injection.

3. Clean the skin as instructed.

4. Stabilise the skin by spreading it or pinching up a large area. Insert the needle and inject as instructed.

5. Pull the needle out and apply gentle pressure over the injection site for several seconds. Do not rub the area.

6. Using the outer needle cap, unscrew the needle and dispose of it safely.

7. Use of injection sites should be rotated so that the same site is not used more than approximately once a month.

Any unused product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORIZATION HOLDER

Eli Lilly Nederland B.V., Orteliuslaan 1000, 3528 BD Utrecht, The Netherlands.

8. MARKETING AUTHORISATION NUMBERS

EU/1/96/007/006
EU/1/96/007/025
EU/1/96/007/035
EU/1/96/007/036

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 30th April 1996
Date of last renewal: 30th April 2006

10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency https://www.ema.europa.eu

1. NAME OF THE MEDICINAL PRODUCT

Humalog 200 units/ml KwikPen solution for injection in a pre-filled pen

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains 200 units insulin lispro*(equivalent to 6.9 mg).

Each pre-filled pen contains 600 units of insulin lispro in 3 ml solution.

Each KwikPen delivers 1-60 units in steps of 1 unit.

* produced in *E.coli* by recombinant DNA technology.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection.

Clear, colourless, aqueous solution.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

For the treatment of adults with diabetes mellitus who require insulin for the maintenance of normal glucose homeostasis. Humalog 200 units/ml KwikPen is also indicated for the initial stabilisation of diabetes mellitus.

4.2 Posology and method of administration

Posology

The dosage should be determined by the physician, according to the requirement of the patient.

Humalog may be given shortly before meals. When necessary Humalog can be given soon after meals.

Humalog takes effect rapidly and has a shorter duration of activity (2 to 5 hours) given subcutaneously as compared with soluble insulin. This rapid onset of activity allows a Humalog injection to be given very close to mealtime. The time course of action of any insulin may vary considerably in different individuals or at different times in the same individual. The faster onset of action compared to soluble human insulin is maintained regardless of injection site. The duration of action of Humalog is dependent on dose, site of injection, blood supply, temperature, and physical activity.

Humalog can be used in conjunction with a longer-acting insulin or oral sulphonylurea medicinal products, on the advice of a physician.

Humalog KwikPens

Humalog KwikPen is available in two strengths.The Humalog 200 units/ml KwikPen (and Humalog 100 units/ml KwikPen, *see separate SmPC*) delivers 1 – 60 units in steps of 1 unit in a single injection. **The number of insulin units is shown in the dose window of the pen regardless of strength** and **no**

dose conversion should be done when transferring a patient to a new strength or to a pen with a different dose step.

Humalog 200 units/ml KwikPen should be reserved for the treatment of patients with diabetes requiring daily doses of more than 20 units of rapid-acting insulin. The insulin lispro solution containing 200 units/ml should not be withdrawn from the pre-filled pen (the KwikPen) or mixed with any other insulin (see section 4.4 and section 6.2).

Special populations

Renal impairment
Insulin requirements may be reduced in the presence of renal impairment.

Hepatic impairment
Insulin requirements may be reduced in patients with hepatic impairment due to reduced capacity for gluconeogenesis and reduced insulin breakdown; however, in patients with chronic hepatic impairment, an increase in insulin resistance may lead to increased insulin requirements.

Method of administration

Humalog solution for injection should be given subcutaneously.

Subcutaneous administration should be in the upper arms, thighs, buttocks, or abdomen. Use of injection sites should be rotated so that the same site is not used more than approximately once a month, in order to reduce the risk of lipodystrophy and cutaneous amyloidosis (see section 4.4 and 4.8).

When administered subcutaneously care should be taken when injecting Humalog to ensure that a blood vessel has not been entered. After injection, the site of injection should not be massaged. Patients must be educated to use the proper injection techniques.

Humalog 200 units/ml KwikPen solution for injection should not be used in an insulin infusion pump.

Humalog 200 units/ml KwikPen solution for injection should not be used intravenously.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

Hypoglycaemia.

4.4 Special warnings and precautions for use

Traceability

In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.

Transferring a patient to another type or brand of insulin

Transferring a patient to another type or brand of insulin should be done under strict medical supervision. Changes in strength, brand (manufacturer), type (regular/soluble, NPH/isophane, etc.), species (animal, human, human insulin analogue), and/or method of manufacture (recombinant DNA *versus* animal-source insulin) may result in the need for a change in dosage. For fast-acting insulins, any patient also on basal insulin must optimise dosage of both insulins to obtain glucose control across the whole day, particularly nocturnal/fasting glucose control.

Hypoglycaemia and hyperglycaemia

Conditions which may make the early warning symptoms of hypoglycaemia different or less pronounced include long duration of diabetes, intensified insulin therapy, diabetic nerve disease or medicinal products such as beta-blockers.

A few patients who have experienced hypoglycaemic reactions after transfer from animal-source insulin to human insulin have reported that the early warning symptoms of hypoglycaemia were less pronounced or different from those experienced with their previous insulin. Uncorrected hypoglycaemic or hyperglycaemic reactions can cause loss of consciousness, coma, or death.

The use of dosages which are inadequate or discontinuation of treatment, especially in insulin-dependent diabetics, may lead to hyperglycaemia and diabetic ketoacidosis; conditions which are potentially lethal.

Injection technique

Patients must be instructed to perform continuous rotation of the injection site to reduce the risk of developing lipodystrophy and cutaneous amyloidosis. There is a potential risk of delayed insulin absorption and worsened glycaemic control following insulin injections at sites with these reactions. A sudden change in the injection site to an unaffected area has been reported to result in hypoglycaemia. Blood glucose monitoring is recommended after the change in the injection site, and dose adjustment of antidiabetic medications may be considered.

Insulin requirements and dosage adjustment

Insulin requirements may be increased during illness or emotional disturbances.
Adjustment of dosage may also be necessary if patients undertake increased physical activity or change their usual diet. Exercise taken immediately after a meal may increase the risk of hypoglycaemia. A consequence of the pharmacodynamics of rapid-acting insulin analogues is that if hypoglycaemia occurs, it may occur earlier after an injection when compared with soluble human insulin.

Combination of Humalog with pioglitazone

Cases of cardiac failure have been reported when pioglitazone was used in combination with insulin, especially in patients with risk factors for development of cardiac heart failure. This should be kept in mind, if treatment with the combination of pioglitazone and Humalog is considered. If the combination is used, patients should be observed for signs and symptoms of heart failure, weight gain and oedema. Pioglitazone should be discontinued, if any deterioration in cardiac symptoms occurs.

Avoidance of medication errors when using insulin lispro (200 units/ml) in pre-filled pen:

The insulin lispro solution for injection containing 200 units/ml must not be transferred from the pre-filled pen, the KwikPen, to a syringe. The markings on the insulin syringe will not measure the dose correctly. Overdose can result causing severe hypoglycemia. The insulin lispro solution for injection containing 200 units/ml must not be transferred from the KwikPen to any other insulin delivery device, including insulin infusion pumps.
Patients must be instructed to always check the insulin label before each injection to avoid accidental mix-ups between the two different strengths of Humalog as well as other insulin products.

Patients must visually verify the dialled units on the dose counter of the pen. Therefore, the requirement for patients to self-inject is that they can read the dose counter on the pen. Patients who are blind or have poor vision must be instructed to always get help/assistance from another person who has good vision and is trained in using the insulin device.

Excipients

This medicinal product contains less than 1 mmol sodium (23 mg) per dose, i.e., essentially "sodium-free".

4.5 Interaction with other medicinal products and other forms of interaction

Insulin requirements may be increased by medicinal products with hyperglycaemic activity, such as oral contraceptives, corticosteroids, or thyroid replacement therapy, danazol, beta2 stimulants (such as ritodrine, salbutamol, terbutaline).

Insulin requirements may be reduced in the presence of medicinal products with hypoglycaemic activity, such as oral hypoglycemics, salicylates (for example, acetylsalicylic acid), sulpha antibiotics, certain antidepressants (monoamine oxidase inhibitors, selective serotonin reuptake inhibitors), certain angiotensin converting enzyme inhibitors (captopril, enalapril), angiotensin II receptor blockers, beta-blockers, octreotide or alcohol.

The physician should be consulted when using other medicinal products in addition to Humalog 200 units/ml KwikPen (see section 4.4).

4.6 Fertility, pregnancy and lactation

Pregnancy

Data on a large number of exposed pregnancies do not indicate any adverse effect of insulin lispro on pregnancy or on the health of the foetus/newborn.

It is essential to maintain good control of the insulin-treated (insulin-dependent or gestational diabetes) patient throughout pregnancy. Insulin requirements usually fall during the first trimester and increase during the second and third trimesters. Patients with diabetes should be advised to inform their doctor if they are pregnant or are contemplating pregnancy. Careful monitoring of glucose control, as well as general health, is essential in pregnant patients with diabetes.

Breast-feeding

Patients with diabetes who are breast-feeding may require adjustments in insulin dose, diet or both.

Fertility

Insulin lispro did not induce fertility impairment in animal studies (see section 5.3).

4.7 Effects on ability to drive and use machines

The patient's ability to concentrate and react may be impaired as a result of hypoglycaemia. This may constitute a risk in situations where these abilities are of special importance (e.g. driving a car or using machines).

Patients should be advised to take precautions to avoid hypoglycaemia whilst driving. This is particularly important in those who have reduced or absent awareness of the warning signs of hypoglycaemia or have frequent episodes of hypoglycaemia. The advisability of driving should be considered in these circumstances.

4.8 Undesirable effects

Summary of safety profile

Hypoglycaemia is the most frequent adverse reaction of insulin lispro therapy that a patient with diabetes may suffer. Severe hypoglycaemia may lead to loss of consciousness, and in extreme cases, death. No specific frequency for hypoglycaemia is presented, since hypoglycaemia is a result of both the insulin dose and other factors e.g. a patient`s level of diet and exercise.

Tabulated list of adverse reactions

The following related adverse reactions from clinical trials are listed below as MedDRA preferred term by system organ class and in order of decreasing incidence (very common: ≥1/10; common: ≥1/100 to <1/10; uncommon: ≥1/1,000 to <1/100; rare: ≥1/10,000 to <1/1,000; very rare: <1/10,000) ; not known (cannot be estimated form the available data).

Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.

MedDRA system organ classes	**Very common**	**Common**	**Uncommon**	**Rare**	**Very rare**	**Not known**
Immune system disorders						
Local allergy		X				
Systemic allergy				X		
Skin and subcutaneous tissue disorders						
Lipodystrophy			X			
Cutaneous amyloidosis						X

Description of selected adverse reactions

Local allergy

Local allergy in patients is common). Redness, swelling, and itching can occur at the site of insulin injection. This condition usually resolves in a few days to a few weeks. In some instances, this condition may be related to factors other than insulin, such as irritants in the skin cleansing agent or poor injection technique.

Systemic allergy

Systemic allergy, which is rare but potentially more serious, is a generalised allergy to insulin. It may cause a rash over the whole body, shortness of breath, wheezing, reduction in blood pressure, fast pulse, or sweating. Severe cases of generalised allergy may be life-threatening.

Skin and subcutaneous tissue disorders

Lipodystrophy and cutaneous amyloidosis may occur at the injection site and delay local insulin absorption. Continuous rotation of the injection site within the given injection area may help to reduce or prevent these reactions (see section 4.4).

Oedema

Cases of oedema have been reported with insulin therapy, particularly if previous poor metabolic control is improved by intensified insulin therapy.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V.

4.9 Overdose

Insulins have no specific overdose definitions because serum glucose concentrations are a result of complex interactions between insulin levels, glucose availability and other metabolic processes. Hypoglycaemia may occur as a result of an excess of insulin activity relative to food intake and energy expenditure.

Hypoglycaemia may be associated with listlessness, confusion, palpitations, headache, sweating and vomiting.

Mild hypoglycaemic episodes will respond to oral administration of glucose or other sugar or saccharated products.

Correction of moderately severe hypoglycaemia can be accomplished by intramuscular or subcutaneous administration of glucagon, followed by oral carbohydrate when the patient recovers sufficiently. Patients who fail to respond to glucagon must be given glucose solution intravenously.

If the patient is comatose, glucagon should be administered intramuscularly or subcutaneously. However, glucose solution must be given intravenously if glucagon is not available or if the patient fails to respond to glucagon. The patient should be given a meal as soon as consciousness is recovered.

Sustained carbohydrate intake and observation may be necessary because hypoglycaemia may recur after apparent clinical recovery.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group : Drugs used in diabetes, insulins and analogues for injection, fast-acting, ATC code: A10AB04

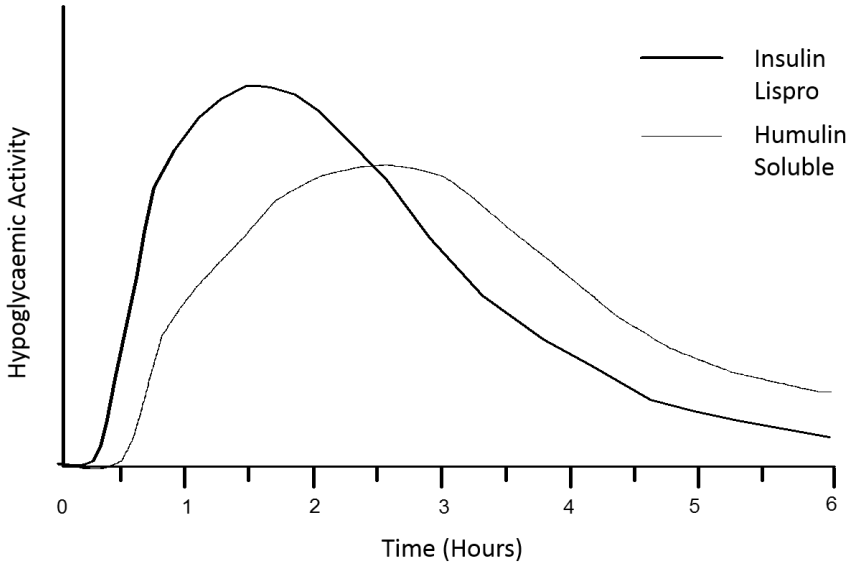
The primary activity of insulin lispro is the regulation of glucose metabolism.

In addition, insulins have several anabolic and anti-catabolic actions on a variety of different tissues. Within muscle tissue this includes increasing glycogen, fatty acid, glycerol and protein synthesis and amino acid uptake, while decreasing glycogenolysis, gluconeogenesis, ketogenesis, lipolysis, protein catabolism and amino acid output.

Insulin lispro has a rapid onset of action (approximately 15 minutes), thus allowing it to be given closer to a meal (within zero to 15 minutes of the meal) when compared to soluble insulin (30 to 45 minutes before). Insulin lispro takes effect rapidly and has a shorter duration of activity (2 to 5 hours) when compared to soluble insulin.

Clinical trials in patients with type 1 and type 2 diabetes have demonstrated reduced postprandial hyperglycaemia with insulin lispro compared to soluble human insulin.
The time course of insulin lispro action may vary in different individuals or at different times in the same individual and is dependent on dose, site of injection, blood supply, temperature and physical activity. The typical activity profile following subcutaneous injection is illustrated below.

Figure 1:



The above representation (figure 1) reflects the relative amount of glucose over time required to maintain the subject's whole blood glucose concentrations near fasting levels and is an indicator of the effect of these insulins (100 units/ml) on glucose metabolism over time.

The pharmacodynamic responses of insulin lispro 200 units/ml solution for injection were similar to those for insulin lispro 100 units/ml solution for injection after subcutaneous administration of a single 20 unit dose in healthy subjects as shown in the graph below (figure 2).

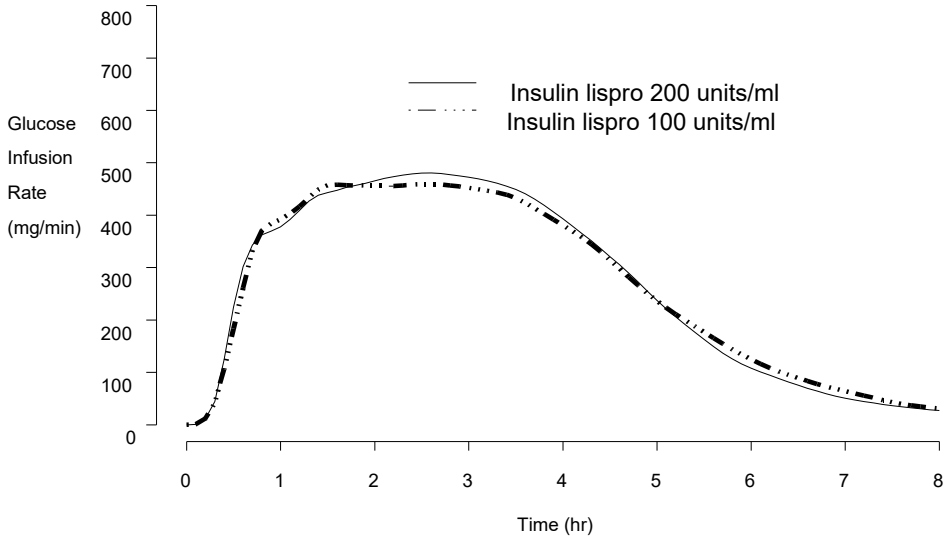


Figure 2: Arithmetic mean glucose infusion rate versus time profiles following subcutaneous administration of 20 units of insulin lispro 200 units/ml or insulin lispro 100 units/ml

In patients with type 2 diabetes on maximum doses of sulphonyl urea agents, studies have shown that the addition of insulin lispro significantly reduces HbA1c compared to sulphonyl urea alone. The reduction of HbA1c would also be expected with other insulin products e.g. soluble or isophane insulins.

Clinical trials in patients with type 1 and type 2 diabetes have demonstrated a reduced number of episodes of nocturnal hypoglycaemia with insulin lispro compared to soluble human insulin. In some studies, reduction of nocturnal hypoglycaemia was associated with increased episodes of daytime hypoglycaemia.

The glucodynamic response to insulin lispro is not affected by renal or hepatic function impairment. Glucodynamic differences between insulin lispro and soluble human insulin, as measured during a glucose clamp procedure, were maintained over a wide range of renal function.

Insulin lispro has been shown to be equipotent to human insulin on a molar basis but its effect is more rapid and of a shorter duration.

5.2 Pharmacokinetic properties

The pharmacokinetics of insulin lispro reflect a compound that is rapidly absorbed, and achieves peak blood levels 30 to 70 minutes following subcutaneous injection. When considering the clinical relevance of these kinetics, it is more appropriate to examine the glucose utilisation curves (as discussed in 5.1).

Insulin lispro maintains more rapid absorption when compared to soluble human insulin in patients with renal impairment. In patients with type 2 diabetes over a wide range of renal function the pharmacokinetic differences between insulin lispro and soluble human insulin were generally maintained and shown to be independent of renal function. Insulin lispro maintains more rapid absorption and elimination when compared to soluble human insulin in patients with hepatic impairment.

Insulin lispro 200 units/ml solution for injection was bioequivalent to insulin lispro 100 units/ml solution for injection after subcutaneous administration of a single 20 unit dose in healthy subjects. Time to maximum concentration was also similar between formulations.

5.3 Preclinical safety data

In *in vitro* tests, including binding to insulin receptor sites and effects on growing cells, insulin lispro behaved in a manner that closely resembled human insulin. Studies also demonstrate that the dissociation of binding to the insulin receptor of insulin lispro is equivalent to human insulin. Acute, one month and twelve month toxicology studies produced no significant toxicity findings.

Insulin lispro did not induce fertility impairment, embryotoxicity or teratogenicity in animal studies.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

m-Cresol
Glycerol
Trometamol
Zinc oxide
Water for injections
Hydrochloric acid and sodium hydroxide may be used to adjust pH.

6.2 Incompatibilities

This medicinal product should not be mixed with any other insulin or any other medicinal product. The solution for injection should not be diluted.

6.3 Shelf life

Before use

3 years.

After first use

28 days.

6.4 Special precautions for storage

Do not freeze. Do not expose to excessive heat or direct sunlight.

Before use

Store in a refrigerator (2°C - 8°C).

After first use

Store below 30°C. Do not refrigerate. The pre-filled pen should not be stored with the needle attached.

6.5 Nature and contents of container

Type I glass cartridges, sealed with halobutyl disc seals and plunger heads and secured with aluminium seals. Dimeticone or silicone emulsion may be used to treat the cartridge plunger, and/or the glass cartridge. The 3 ml cartridges which contain 600 units insulin lispro (200 units/ml), are sealed in a disposable pen injector, called the "KwikPen". Needles are not included.

1 pre-filled pen of 3 ml
2 pre-filled pens of 3 ml
5 pre-filled pens of 3 ml
Multipacks containing 10 (2 packs of 5) pre-filled pens of 3 ml

Not all packs may be marketed.

6.6 Special precautions for disposal and other handling

Instructions for use and handling

To prevent the possible transmission of disease, each pen must be used by one patient only, even if the needle is changed. The patient should discard the needle after every injection.

The Humalog solution should be clear and colourless. Humalog should not be used if it appears cloudy, thickened, or slightly coloured or if solid particles are visible.

Handling of the pre-filled pen

Before using the KwikPen the user manual included in the package leaflet must be read carefully. The KwikPen has to be used as recommended in the user manual.

Pens should not be used if any part looks broken or damaged.

Any unused product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Eli Lilly Nederland B.V., Orteliuslaan 1000, 3528 BD Utrecht, The Netherlands.

8. MARKETING AUTHORISATION NUMBERS

EU/1/96/007/039
EU/1/96/007/040
EU/1/96/007/041
EU/1/96/007/042

9. DATE OF FIRST AUTHORISATION / RENEWAL OF THE AUTHORISATION

Date of first authorisation: 30th April 1996
Date of last renewal: 30th April 2006

10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency https://www.ema.europa.eu

ANNEX II

A. MANUFACTURERS OF THE BIOLOGICAL ACTIVE SUBSTANCE AND MANUFACTURERS RESPONSIBLE FOR BATCH RELEASE

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

A. MANUFACTURERS OF THE BIOLOGICAL ACTIVE SUBSTANCE AND MANUFACTURERS RESPONSIBLE FOR BATCH RELEASE

Names and addresses of the manufacturers of the biological active substance

Fermentation
Eli Lilly and Company, Lilly Technology Center Building 333 and 324, Indianapolis, Indiana, USA
Lilly del Caribe, Inc., Puerto Rico Industrial Park, 12.3 KM (PR05), 65th Infantry Road, Carolina, Puerto Rico 00985

Granule Recovery
Eli Lilly and Company, Lilly Technology Center Building 130, Indianapolis, Indiana, USA
Lilly del Caribe, Inc., Puerto Rico Industrial Park, 12.3 KM (PR05), 65th Infantry Road, Carolina, Puerto Rico 00985

Names and addresses of the manufacturers responsible for batch release

Vials
Lilly S.A., Avda. de la Industria 30, 28108 Alcobendas, Madrid, Spain.

Cartridges
Lilly France S.A.S., Rue du Colonel Lilly, 67640 Fegersheim, France.
Eli Lilly Italia S.p.A., Via Gramsci 731-733, 50019 Sesto Fiorentino, (FI) Italy.

Humalog 100 units/ml KwikPen, Humalog Mix25 100 units/ml KwikPen, Humalog Mix50 100 units/ml KwikPen and Humalog 200 units/ml KwikPen
Lilly France S.A.S., Rue du Colonel Lilly, 67640 Fegersheim, France.
Eli Lilly Italia S.p.A., Via Gramsci 731-733, 50019 Sesto Fiorentino, (FI) Italy.

Humalog 100 units/ml Junior KwikPen and Humalog 100 units/ml Tempo Pen
Lilly France S.A.S., Rue du Colonel Lilly, 67640 Fegersheim, France.

The printed package leaflet of the medicinal product must state the name and address of the manufacturer responsible for the release of the concerned batch

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product subject to medical prescription

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

- **Periodic safety update reports (PSURs)**

The requirements for submission of PSURs for this medicinal product are set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and any subsequent updates published on the European medicines web-portal.

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

- **Risk management plan (RMP)**

The marketing authorisation holder (MAH) shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the marketing authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:

- At the request of the European Medicines Agency;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON – Vial. Pack of 1 and 2

1. NAME OF THE MEDICINAL PRODUCT

Humalog 100 units/ml solution for injection in vial
insulin lispro

2. STATEMENT OF ACTIVE SUBSTANCE

One ml solution contains 100 units of insulin lispro (equivalent to 3.5mg).

3. LIST OF EXCIPIENTS

Contains glycerol, zinc oxide, dibasic sodium phosphate $7H_20$ with m-cresol as a preservative in water for injection.
Sodium hydroxide and/or hydrochloric acid may have been used to adjust acidity. See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection

1 vial of 10 ml
2 vials of 10 ml

5. METHOD AND ROUTES OF ADMINISTRATION

Read the package leaflet before use.
Subcutaneous and intravenous use

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children

7. OTHER SPECIAL WARNING, IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator (2°C - 8°C).
Do not freeze. Do not expose to excessive heat or direct sunlight.
Once in use, vials may be used for up to 28 days. Vials in use should be stored below 30°C.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Eli Lilly Nederland B.V.
Orteliuslaan 1000, 3528 BD Utrecht
The Netherlands

12. MARKETING AUTHORISATION NUMBERS

EU/1/96/007/002
EU/1/96/007/020

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON (with blue box) multipack – Vial

1. NAME OF THE MEDICINAL PRODUCT

Humalog 100 units/ml solution for injection in vial
insulin lispro

2. STATEMENT OF ACTIVE SUBSTANCE

One ml solution contains 100 units of insulin lispro (equivalent to 3.5mg).

3. LIST OF EXCIPIENTS

Contains glycerol, zinc oxide, dibasic sodium phosphate $7H_20$ with m-cresol as a preservative in water for injection.
Sodium hydroxide and/or hydrochloric acid may have been used to adjust acidity. See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection.

Multipack: 5 (5 packs of 1) vials of 10 ml.

5. METHOD AND ROUTES OF ADMINISTRATION

Read the package leaflet before use.
Subcutaneous and intravenous use

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children

7. OTHER SPECIAL WARNING, IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator (2°C - 8°C).

Do not freeze. Do not expose to excessive heat or direct sunlight.
Once in use, vials may be used for up to 28 days. Vials in use should be stored below 30°C.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Eli Lilly Nederland B.V.
Orteliuslaan 1000, 3528 BD Utrecht
The Netherlands

12. MARKETING AUTHORISATION NUMBER

EU/1/96/007/021

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

INTERMEDIATE CARTON (without blue box) component of a multipack – Vial

1. NAME OF THE MEDICINAL PRODUCT

Humalog 100 units/ml solution for injection in vial
insulin lispro

2. STATEMENT OF ACTIVE SUBSTANCE

One ml solution contains 100 units of insulin lispro (equivalent to 3.5mg).

3. LIST OF EXCIPIENTS

Contains glycerol, zinc oxide, dibasic sodium phosphate $7H_20$ with m-cresol as a preservative in water for injection.
Sodium hydroxide and/or hydrochloric acid may have been used to adjust acidity. See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection

1 vial of 10 ml. Component of a multipack, can't be sold separately.

5. METHOD AND ROUTES OF ADMINISTRATION

Read the package leaflet before use.
Subcutaneous and intravenous use

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children

7. OTHER SPECIAL WARNING, IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator (2°C - 8°C).
Do not freeze. Do not expose to excessive heat or direct sunlight.
Once in use, vials may be used for up to 28 days. Vials in use should be stored below 30°C.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Eli Lilly Nederland B.V.
Orteliuslaan 1000, 3528 BD Utrecht
The Netherlands

12. MARKETING AUTHORISATION NUMBER

EU/1/96/007/021

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

17. UNIQUE IDENTIFIER – 2D BARCODE

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

LABEL TEXT

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE OF ADMINISTRATION

Humalog 100 units/ml solution for injection in vial
insulin lispro
Subcutaneous and intravenous use

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

10 ml (3.5 mg/ml)

6. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON - Cartridges. Pack of 5 and 10

1. NAME OF THE MEDICINAL PRODUCT

Humalog 100 units/ml solution for injection in cartridge
insulin lispro

2. STATEMENT OF ACTIVE SUBSTANCE

One ml solution contains 100 units of insulin lispro (equivalent to 3.5mg).

3. LIST OF EXCIPIENTS

Contains glycerol, zinc oxide, dibasic sodium phosphate$7H_20$ with m-cresol as a preservative in water for injection.
Sodium hydroxide and/or hydrochloric acid may have been used to adjust acidity. See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection

5 cartridges of 3 ml
10 cartridges of 3 ml

5. METHOD AND ROUTES OF ADMINISTRATION

Read the package leaflet before use.
Subcutaneous use

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children

7. OTHER SPECIAL WARNINGS, IF NECESSARY

These cartridges are for use with a Lilly 3 ml pen only.

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator (2°C - 8°C).
Do not freeze. Do not expose to excessive heat or direct sunlight.
Once in use cartridges may be used for up to 28 days. Following insertion in a pen, the cartridge and pen should be stored below 30°C and should not be refrigerated.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Eli Lilly Nederland B.V.
Orteliuslaan 1000, 3528 BD Utrecht
The Netherlands

12. MARKETING AUTHORISATION NUMBERS

EU/1/96/007/004
EU/1/96/007/023

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

(To open, lift here and pull)
CARTON HAS BEEN OPENED

16. INFORMATION IN BRAILLE

Humalog

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

LABEL TEXT

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE OF ADMINISTRATION

Humalog 100 units/ml solution for injection in cartridge
insulin lispro
Subcutaneous use

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

3 ml (3.5 mg/ml)

6. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON – Vial. Pack of 1

1. NAME OF THE MEDICINAL PRODUCT

Humalog Mix25 100 units/ml suspension for injection in vial
25% insulin lispro and 75% insulin lispro protamine suspension

2. STATEMENT OF ACTIVE SUBSTANCE

One ml suspension contains 100 units of insulin lispro (equivalent to 3.5mg).

3. LIST OF EXCIPIENTS

Contains protamine sulphate, glycerol, zinc oxide, dibasic sodium phosphate.$7H_2O$ with m-cresol and phenol as preservatives in water for injections.
Sodium hydroxide and/or hydrochloric acid may have been used to adjust acidity. See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Suspension for injection

1 vial of 10 ml

5. METHOD AND ROUTE OF ADMINISTRATION

Read the package leaflet before use.
Subcutaneous use

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children

7. OTHER SPECIAL WARNINGS, IF NECESSARY

Resuspend carefully. See enclosed package leaflet.

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator (2°C - 8°C).
Do not freeze. Do not expose to excessive heat or direct sunlight.
Once in use, vials may be used for up to 28 days. Vials in use should be stored below 30°C.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Eli Lilly Nederland B.V.
Orteliuslaan 1000, 3528 BD Utrecht
The Netherlands

12. MARKETING AUTHORISATION NUMBER

EU/1/96/007/005

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

LABEL TEXT

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE OF ADMINISTRATION

Humalog Mix25 100 units/ml suspension for injection in vial
25% insulin lispro and 75% insulin lispro protamine suspension
Subcutaneous use

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

10 ml (3.5 mg/ml)

6. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON – Cartridges. Pack of 5 and 10

1. NAME OF THE MEDICINAL PRODUCT

Humalog Mix25 100 units/ml suspension for injection in cartridge
25% insulin lispro and 75% insulin lispro protamine suspension

2. STATEMENT OF ACTIVE SUBSTANCE

One ml suspension contains 100 units of insulin lispro (equivalent to 3.5mg).

3. LIST OF EXCIPIENTS

Contains protamine sulphate, glycerol, zinc oxide, dibasic sodium phosphate 7 H_20 with m-cresol and phenol as preservatives in water for injections.
Sodium hydroxide and/or hydrochloric acid may have been used to adjust acidity. See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Suspension for injection

5 cartridges of 3 ml
10 cartridges of 3 ml

5. METHOD AND ROUTE OF ADMINISTRATION

Read the package leaflet before use.
Subcutaneous use

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children

7. OTHER SPECIAL WARNING, IF NECESSARY

Resuspend carefully. See enclosed package leaflet.
These cartridges are for use with a Lilly 3 ml pen only.

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator (2°C - 8°C).
Do not freeze. Do not expose to excessive heat or direct sunlight.
Once in use cartridges may be used for up to 28 days. Following insertion in a pen, the cartridge and pen should be stored below 30°C and should not be refrigerated.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Eli Lilly Nederland B.V.
Orteliuslaan 1000, 3528 BD Utrecht
The Netherlands

12. MARKETING AUTHORISATION NUMBERS

EU/1/96/007/008
EU/1/96/007/024

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

(To open, lift here and pull)
CARTON HAS BEEN OPENED

16. INFORMATION IN BRAILLE

Humalog Mix25

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

LABEL TEXT

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE OF ADMINISTRATION

Humalog Mix25 100 units/ml suspension for injection in cartridge
25% insulin lispro and 75% insulin lispro protamine suspension
Subcutaneous use

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

3 ml (3.5 mg/ml)

6. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON – Cartridges. Pack of 5 and 10

1. NAME OF THE MEDICINAL PRODUCT

Humalog Mix50 100 units/ml suspension for injection in cartridge
50% insulin lispro and 50% insulin lispro protamine suspension

2. STATEMENT OF ACTIVE SUBSTANCE

One ml suspension contains 100 units of insulin lispro (equivalent to 3.5mg).

3. LIST OF EXCIPIENTS

Contains protamine sulphate, glycerol, zinc oxide, dibasic sodium phosphate 7 H_20 with m-cresol and phenol as preservatives in water for injections.
Sodium hydroxide and/or hydrochloric acid may have been used to adjust acidity. See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Suspension for injection

5 cartridges of 3 ml
10 cartridges of 3 ml

5. METHOD AND ROUTE OF ADMINISTRATION

Read the package leaflet before use.
Subcutaneous use

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children

7. OTHER SPECIAL WARNING, IF NECESSARY

Resuspend carefully. See enclosed package leaflet.
These cartridges are for use with a Lilly 3 ml pen only.

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator (2°C - 8°C).
Do not freeze. Do not expose to excessive heat or direct sunlight.
Once in use cartridges may be used for up to 28 days. Following insertion in a pen, the cartridge and pen should be stored below 30°C and should not be refrigerated.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Eli Lilly Nederland B.V.
Orteliuslaan 1000, 3528 BD Utrecht
The Netherlands

12. MARKETING AUTHORISATION NUMBERS

EU/1/96/007/006
EU/1/96/007/025

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

(To open, lift here and pull)
CARTON HAS BEEN OPENED

16. INFORMATION IN BRAILLE

Humalog Mix50

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

LABEL TEXT

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE OF ADMINISTRATION

Humalog Mix50 100 units/ml suspension for injection in cartridge
50% insulin lispro and 50% insulin lispro protamine suspension
Subcutaneous use

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

3 ml (3.5 mg/ml)

6. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON – KwikPen. Pack of 5

1. NAME OF THE MEDICINAL PRODUCT

Humalog 100 units/ml KwikPen solution for injection in a pre-filled pen.
insulin lispro

2. STATEMENT OF ACTIVE SUBSTANCE

One ml solution contains 100 units of insulin lispro (equivalent to 3.5mg).

3. LIST OF EXCIPIENTS

Contains glycerol, zinc oxide, dibasic sodium phosphate 7 H_20 with m-cresol as a preservative in water for injections.
Sodium hydroxide and/or hydrochloric acid may have been used to adjust acidity. See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection.

5 pens of 3 ml

5. METHOD AND ROUTES OF ADMINISTRATION

Read the package leaflet before use.
Subcutaneous use

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children

7. OTHER SPECIAL WARNING, IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator (2°C - 8°C).
Do not freeze. Do not expose to excessive heat or direct sunlight.
Once in use pens may be used for up to 28 days. Pens in use should be stored below 30°C and should not be refrigerated.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Eli Lilly Nederland B.V.
Orteliuslaan 1000, 3528 BD Utrecht
The Netherlands

12. MARKETING AUTHORISATION NUMBER

EU/1/96/007/031

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

If seal is broken before first use, contact pharmacist.

16. INFORMATION IN BRAILLE

Humalog KwikPen

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON (with blue box) multipack – KwikPen

1. NAME OF THE MEDICINAL PRODUCT

Humalog 100 units/ml KwikPen solution for injection in a pre-filled pen
insulin lispro

2. STATEMENT OF ACTIVE SUBSTANCE

One ml solution contains 100 units of insulin lispro (equivalent to 3.5mg).

3. LIST OF EXCIPIENTS

Contains glycerol, zinc oxide, dibasic sodium phosphate 7 H_20 with m-cresol as a preservative in water for injections.
Sodium hydroxide and/or hydrochloric acid may have been used to adjust acidity. See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection.

Multipack: 10 (2 packs of 5) pens of 3 ml.

5. METHOD AND ROUTES OF ADMINISTRATION

Read the package leaflet before use
Subcutaneous use

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children

7. OTHER SPECIAL WARNING, IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator (2°C - 8°C).
Do not freeze. Do not expose to excessive heat or direct sunlight.

Once in use pens may be used for up to 28 days. Pens in use should be stored below 30°C and should not be refrigerated.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Eli Lilly Nederland B.V.
Orteliuslaan 1000, 3528 BD Utrecht
The Netherlands

12. MARKETING AUTHORISATION NUMBER

EU/1/96/007/032

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Humalog KwikPen

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

INTERMEDIATE CARTON (without blue box) component of a multipack – KwikPen

1. NAME OF THE MEDICINAL PRODUCT

Humalog 100 units/ml KwikPen solution for injection in a pre-filled pen
insulin lispro

2. STATEMENT OF ACTIVE SUBSTANCE

One ml solution contains 100 units of insulin lispro (equivalent to 3.5mg).

3. LIST OF EXCIPIENTS

Contains glycerol, zinc oxide, dibasic sodium phosphate 7 H_20 with m-cresol as a preservative in water for injections.
Sodium hydroxide and/or hydrochloric acid may have been used to adjust acidity. See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection..

5 pens of 3 ml. Component of a multipack, can't be sold separately.

5. METHOD AND ROUTES OF ADMINISTRATION

Read the package leaflet before use.
Subcutaneous use

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children

7. OTHER SPECIAL WARNING, IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator (2°C - 8°C).
Do not freeze. Do not expose to excessive heat or direct sunlight.
Once in use pens may be used for up to 28 days. Pens in use should be stored below 30°C and should not be refrigerated.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Eli Lilly Nederland B.V.
Orteliuslaan 1000, 3528 BD Utrecht
The Netherlands

12. MARKETING AUTHORISATION NUMBER

EU/1/96/007/032

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

If seal is broken before first use, contact pharmacist.

16. INFORMATION IN BRAILLE

Humalog KwikPen

17. UNIQUE IDENTIFIER – 2D BARCODE

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

LABEL TEXT

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE OF ADMINISTRATION

Humalog 100 units/ml KwikPen solution for injection
insulin lispro
Subcutaneous use

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

3 ml (3.5 mg/ml)

6. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON – KwikPen. Pack of 5

1. NAME OF THE MEDICINAL PRODUCT

Humalog Mix25 100 units/ml KwikPen suspension for injection in a pre-filled pen
25% insulin lispro and 75% insulin lispro protamine suspension

2. STATEMENT OF ACTIVE SUBSTANCE

One ml suspension contains 100 units of insulin lispro (equivalent to 3.5mg).

3. LIST OF EXCIPIENTS

Contains protamine sulphate, glycerol, zinc oxide, dibasic sodium phosphate 7 H_20 with m-cresol and phenol as preservatives in water for injections.
Sodium hydroxide and/or hydrochloric acid may have been used to adjust acidity. See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Suspension for injection

5 pens of 3 ml

5. METHOD AND ROUTE OF ADMINISTRATION

Read the package leaflet before use.
Subcutaneous use

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children

7. OTHER SPECIAL WARNING, IF NECESSARY

Resuspend carefully. See enclosed package leaflet.

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator (2°C - 8°C).
Do not freeze. Do not expose to excessive heat or direct sunlight.
Once in use pens may be used for up to 28 days. Pens in use should be stored below 30°C and should not be refrigerated.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Eli Lilly Nederland B.V.
Orteliuslaan 1000, 3528 BD Utrecht
The Netherlands

12. MARKETING AUTHORISATION NUMBER

EU/1/96/007/033

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

If seal is broken before first use, contact pharmacist.

16. INFORMATION IN BRAILLE

Humalog Mix25 KwikPen

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON (with blue box) multipack – KwikPen

1. NAME OF THE MEDICINAL PRODUCT

Humalog Mix25 100 units/ml KwikPen suspension for injection in a pre-filled pen
25% insulin lispro and 75% insulin lispro protamine suspension

2. STATEMENT OF ACTIVE SUBSTANCE

One ml suspension contains 100 units of insulin lispro (equivalent to 3.5mg).

3. LIST OF EXCIPIENTS

Contains protamine sulphate, glycerol, zinc oxide, dibasic sodium phosphate 7 H_20 with m-cresol and phenol as preservatives in water for injections.
Sodium hydroxide and/or hydrochloric acid may have been used to adjust acidity. See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Suspension for injection.

Multipack: 10 (2 packs of 5) pens of 3 ml.

5. METHOD AND ROUTES OF ADMINISTRATION

Read the package leaflet before use
Subcutaneous use

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children

7. OTHER SPECIAL WARNING, IF NECESSARY

Resuspend carefully. See enclosed package leaflet.

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator (2°C - 8°C).
Do not freeze. Do not expose to excessive heat or direct sunlight.
Once in use pens may be used for up to 28 days. Pens in use should be stored below 30°C and should not be refrigerated.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Eli Lilly Nederland B.V.
Orteliuslaan 1000, 3528 BD Utrecht
The Netherlands

12. MARKETING AUTHORISATION NUMBER

EU/1/96/007/034

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Humalog Mix25 KwikPen

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

INTERMEDIATE CARTON (without blue box) component of a multipack - KwikPen

1. NAME OF THE MEDICINAL PRODUCT

Humalog Mix25 100 units/ml KwikPen suspension for injection in a pre-filled pen
25% insulin lispro and 75% insulin lispro protamine suspension

2. STATEMENT OF ACTIVE SUBSTANCE

One ml suspension contains 100 units of insulin lispro (equivalent to 3.5mg).

3. LIST OF EXCIPIENTS

Contains protamine sulphate, glycerol, zinc oxide, dibasic sodium phosphate 7 H_20 with m-cresol and phenol as preservatives in water for injections.
Sodium hydroxide and/or hydrochloric acid may have been used to adjust acidity. See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Suspension for injection.

5 pens of 3 ml. Component of a multipack, can't be sold separately.

5. METHOD AND ROUTE OF ADMINISTRATION

Read the package leaflet before use.
Subcutaneous use

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children

7. OTHER SPECIAL WARNING, IF NECESSARY

Resuspend carefully. See enclosed package leaflet.

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator (2°C - 8°C).
Do not freeze. Do not expose to excessive heat or direct sunlight.
Once in use pens may be used for up to 28 days. Pens in use should be stored below 30°C and should not be refrigerated.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Eli Lilly Nederland B.V.
Orteliuslaan 1000, 3528 BD Utrecht
The Netherlands

12. MARKETING AUTHORISATION NUMBER

EU/1/96/007/034

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

If seal is broken before first use, contact pharmacist.

16. INFORMATION IN BRAILLE

Humalog Mix25 KwikPen

17. UNIQUE IDENTIFIER – 2D BARCODE

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

LABEL TEXT

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE OF ADMINISTRATION

Humalog Mix25 100 units/ml KwikPen suspension for injection
25% insulin lispro and 75% insulin lispro protamine suspension
Subcutaneous use

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

3 ml (3.5 mg/ml)

6. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON – KwikPen. Pack of 5

1. NAME OF THE MEDICINAL PRODUCT

Humalog Mix50 100 units/ml KwikPen suspension for injection in a pre-filled pen
50% insulin lispro and 50% insulin lispro protamine suspension

2. STATEMENT OF ACTIVE SUBSTANCE

One ml suspension contains 100 units of insulin lispro (equivalent to 3.5mg).

3. LIST OF EXCIPIENTS

Contains protamine sulphate, glycerol, zinc oxide, dibasic sodium phosphate 7 H_20 with m-cresol and phenol as preservatives in water for injections.
Sodium hydroxide and/or hydrochloric acid may have been used to adjust acidity. See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Suspension for injection.

5 pens of 3 ml

5. METHOD AND ROUTE OF ADMINISTRATION

Read the package leaflet before use.
Subcutaneous use

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children

7. OTHER SPECIAL WARNING, IF NECESSARY

Resuspend carefully. See enclosed package leaflet.

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator (2°C - 8°C).
Do not freeze. Do not expose to excessive heat or direct sunlight.
Once in use pens may be used for up to 28 days. Pens in use should be stored below 30°C and should not be refrigerated.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Eli Lilly Nederland B.V.
Orteliuslaan 1000, 3528 BD Utrecht
The Netherlands

12. MARKETING AUTHORISATION NUMBER

EU/1/96/007/035

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

If seal is broken before first use, contact pharmacist.

16. INFORMATION IN BRAILLE

Humalog Mix50 KwikPen

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON (with blue box) multipack – KwikPen

1. NAME OF THE MEDICINAL PRODUCT

Humalog Mix50 100 units/ml KwikPen suspension for injection in a pre-filled pen
50% insulin lispro and 50% insulin lispro protamine suspension

2. STATEMENT OF ACTIVE SUBSTANCE

One ml suspension contains 100 units of insulin lispro (equivalent to 3.5mg).

3. LIST OF EXCIPIENTS

Contains protamine sulphate, glycerol, zinc oxide, dibasic sodium phosphate 7 H_20 with m-cresol and phenol as preservatives in water for injections.
Sodium hydroxide and/or hydrochloric acid may have been used to adjust acidity. See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Suspension for injection.

Multipack: 10 (2 packs of 5) pens of 3 ml.

5. METHOD AND ROUTES OF ADMINISTRATION

Read the package leaflet before use
Subcutaneous use

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children

7. OTHER SPECIAL WARNING, IF NECESSARY

Resuspend carefully. See enclosed package leaflet.

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator (2°C - 8°C).
Do not freeze. Do not expose to excessive heat or direct sunlight.
Once in use pens may be used for up to 28 days. Pens in use should be stored below 30°C and should not be refrigerated.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Eli Lilly Nederland B.V.
Orteliuslaan 1000, 3528 BD Utrecht
The Netherlands

12. MARKETING AUTHORISATION NUMBER

EU/1/96/007/036

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Humalog Mix50 KwikPen

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

INTERMEDIATE CARTON (without blue box) component of a multipack - KwikPen

1. NAME OF THE MEDICINAL PRODUCT

Humalog Mix50 100 units/ml KwikPen suspension for injection in a pre-filled pen
50% insulin lispro and 50% insulin lispro protamine suspension

2. STATEMENT OF ACTIVE SUBSTANCE

One ml suspension contains 100 units of insulin lispro (equivalent to 3.5mg).

3. LIST OF EXCIPIENTS

Contains protamine sulphate, glycerol, zinc oxide, dibasic sodium phosphate 7 H_20 with m-cresol and phenol as preservatives in water for injections.
Sodium hydroxide and/or hydrochloric acid may have been used to adjust acidity. See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Suspension for injection.

Multipack: 5 pens of 3 ml. Component of a multipack, can't be sold separately.

5. METHOD AND ROUTE OF ADMINISTRATION

Read the package leaflet before use.
Subcutaneous use

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children

7. OTHER SPECIAL WARNING, IF NECESSARY

Resuspend carefully. See enclosed package leaflet.

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator (2°C - 8°C).
Do not freeze. Do not expose to excessive heat or direct sunlight.
Once in use pens may be used for up to 28 days. Pens in use should be stored below 30°C and should not be refrigerated.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Eli Lilly Nederland B.V.
Orteliuslaan 1000, 3528 BD Utrecht
The Netherlands

12. MARKETING AUTHORISATION NUMBER

EU/1/96/007/036

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

If seal is broken before first use, contact pharmacist.

16. INFORMATION IN BRAILLE

Humalog Mix50 KwikPen

17. UNIQUE IDENTIFIER – 2D BARCODE

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

LABEL TEXT

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE OF ADMINISTRATION

Humalog Mix50 100 units/ml KwikPen suspension for injection
50% insulin lispro and 50% insulin lispro protamine suspension
Subcutaneous use

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

3 ml (3.5 mg/ml)

6. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON – KwikPen. Pack of 1, 2 and 5

1. NAME OF THE MEDICINAL PRODUCT

Humalog 200 units/ml KwikPen solution for injection in a pre-filled pen
insulin lispro

2. STATEMENT OF ACTIVE SUBSTANCE

One ml solution contains 200 units of insulin lispro (equivalent to 6.9 mg)

3. LIST OF EXCIPIENTS

Contains glycerol, zinc oxide, trometamol, metacresol and water for injections.
Sodium hydroxide and/or hydrochloric acid may have been used to adjust acidity. See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection.

1 pen of 3 mL.
2 pens of 3 mL.
5 pens of 3 mL.

5. METHOD AND ROUTES OF ADMINISTRATION

Read the package leaflet before use
Subcutaneous use

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children

7. OTHER SPECIAL WARNING, IF NECESSARY

Use only in this pen, or severe overdose can result.
If seal is broken before first use, contact pharmacist.

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator (2°C - 8°C).
Do not freeze. Do not expose to excessive heat or direct sunlight.
Once in use pens may be used for up to 28 days. Pens in use should be stored below 30°C and should not be refrigerated.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Eli Lilly Nederland B.V.
Orteliuslaan 1000, 3528 BD Utrecht
The Netherlands

12. MARKETING AUTHORISATION NUMBERS

EU/1/96/007/039	1 pen
EU/1/96/007/040	2 pens
EU/1/96/007/041	5 pens

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Humalog 200 units/ml

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON (with blue box) multipack – KwikPen

1. NAME OF THE MEDICINAL PRODUCT

Humalog 200 units/ml KwikPen solution for injection in a pre-filled pen
insulin lispro

2. STATEMENT OF ACTIVE SUBSTANCE

One ml solution contains 200 units of insulin lispro (equivalent to 6.9 mg)

3. LIST OF EXCIPIENTS

Contains glycerol, zinc oxide, trometamol, metacresol and water for injections.
Sodium hydroxide and/or hydrochloric acid may have been used to adjust acidity. See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection.

Multipack: 10 (2 packs of 5) pens of 3 ml.

5. METHOD AND ROUTES OF ADMINISTRATION

Read the package leaflet before use
Subcutaneous use

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children

7. OTHER SPECIAL WARNING, IF NECESSARY

Use only in this pen, or severe overdose can result.
If seal is broken before first use, contact pharmacist.

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator (2°C - 8°C).
Do not freeze. Do not expose to excessive heat or direct sunlight.
Once in use pens may be used for up to 28 days. Pens in use should be stored below 30°C and should not be refrigerated.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Eli Lilly Nederland B.V.
Orteliuslaan 1000, 3528 BD Utrecht
The Netherlands

12. MARKETING AUTHORISATION NUMBER

EU/1/96/007/042

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Humalog 200 units/ml

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

INTERMEDIATE CARTON (without blue box) component of a multipack – KwikPen

1. NAME OF THE MEDICINAL PRODUCT

Humalog 200 units/ml KwikPen solution for injection in a pre-filled pen
insulin lispro

2. STATEMENT OF ACTIVE SUBSTANCE

One ml solution contains 200 units of insulin lispro (equivalent to 6.9 mg)

3. LIST OF EXCIPIENTS

Contains glycerol, zinc oxide, trometamol, metacresol and water for injections.
Sodium hydroxide and/or hydrochloric acid may have been used to adjust acidity. See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection.

Multipack: 5 pens of 3 ml. Component of a multipack, can't be sold separately.

5. METHOD AND ROUTES OF ADMINISTRATION

Read the package leaflet before use
Subcutaneous use

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children

7. OTHER SPECIAL WARNING, IF NECESSARY

Use only in this pen, or severe overdose can result.
If seal is broken before first use, contact pharmacist.

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator (2°C - 8°C).
Do not freeze. Do not expose to excessive heat or direct sunlight.
Once in use pens may be used for up to 28 days. Pens in use should be stored below 30°C and should not be refrigerated.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Eli Lilly Nederland B.V.
Orteliuslaan 1000, 3528 BD Utrecht
The Netherlands

12. MARKETING AUTHORISATION NUMBER

EU/1/96/007/042

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Humalog 200 units/ml

17. UNIQUE IDENTIFIER – 2D BARCODE

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

LABEL TEXT

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE OF ADMINISTRATION

Humalog 200 units/ml KwikPen solution for injection
insulin lispro
Subcutaneous use

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

3 ml

6. OTHER

USE ONLY IN THIS PEN, OR SEVERE OVERDOSE CAN RESULT.

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON – Junior KwikPen. Pack of 1 and 5

1. NAME OF THE MEDICINAL PRODUCT

Humalog 100 units/ml Junior KwikPen solution for injection in a pre-filled pen.
insulin lispro

2. STATEMENT OF ACTIVE SUBSTANCE

One ml solution contains 100 units of insulin lispro (equivalent to 3.5 mg).

3. LIST OF EXCIPIENTS

Contains glycerol, zinc oxide, dibasic sodium phosphate$7H_20$, metacresol and water for injections. Sodium hydroxide and/or hydrochloric acid may have been used to adjust acidity. See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection.

1 pen of 3 mL.
5 pens of 3 mL.

5. METHOD AND ROUTES OF ADMINISTRATION

Read the package leaflet before use.
Subcutaneous use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING, IF NECESSARY

The pen delivers 0.5 – 30 units in steps of 0.5 units.

If seal is broken before first use, contact pharmacist.

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator (2°C - 8°C).
Do not freeze. Do not expose to excessive heat or direct sunlight.
Once in use pens may be used for up to 28 days. Discard after 28 days even if some of the solution remains. Pens in use should be stored below 30°C and should not be refrigerated.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Eli Lilly Nederland B.V.
Orteliuslaan 1000, 3528 BD Utrecht
The Netherlands

12. MARKETING AUTHORISATION NUMBERS

EU/1/96/007/043 1 pen
EU/1/96/007/044 5 pens

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Humalog 100 units/ml Junior KwikPen

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON (with blue box) multipack – Junior KwikPen

1. NAME OF THE MEDICINAL PRODUCT

Humalog 100 units/ml Junior KwikPen solution for injection in a pre-filled pen.
insulin lispro

2. STATEMENT OF ACTIVE SUBSTANCE

One ml solution contains 100 units of insulin lispro (equivalent to 3.5 mg).

3. LIST OF EXCIPIENTS

Contains glycerol, zinc oxide, dibasic sodium phosphate$7H_20$, metacresol and water for injections. Sodium hydroxide and/or hydrochloric acid may have been used to adjust acidity. See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection.

Multipack: 10 (2 packs of 5) pens of 3 ml.

5. METHOD AND ROUTES OF ADMINISTRATION

Read the package leaflet before use.
Subcutaneous use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children

7. OTHER SPECIAL WARNING, IF NECESSARY

The pen delivers 0.5 – 30 units in steps of 0.5 units.

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator (2°C - 8°C).
Do not freeze. Do not expose to excessive heat or direct sunlight.
Once in use pens may be used for up to 28 days. Discard after 28 days even if some of the solution remains. Pens in use should be stored below 30°C and should not be refrigerated.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Eli Lilly Nederland B.V.
Orteliuslaan 1000, 3528 BD Utrecht
The Netherlands

12. MARKETING AUTHORISATION NUMBER

EU/1/96/007/045

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Humalog 100 units/ml Junior KwikPen

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

INTERMEDIATE CARTON (without blue box) component of a multipack – Junior KwikPen

1. NAME OF THE MEDICINAL PRODUCT

Humalog 100 units/ml Junior KwikPen solution for injection in a pre-filled pen.
insulin lispro

2. STATEMENT OF ACTIVE SUBSTANCE

One ml solution contains 100 units of insulin lispro (equivalent to 3.5 mg).

3. LIST OF EXCIPIENTS

Contains glycerol, zinc oxide, dibasic sodium phosphate$7H_20$, metacresol and water for injections. Sodium hydroxide and/or hydrochloric acid may have been used to adjust acidity. See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection.

Multipack: 5 pens of 3 ml. Component of a multipack, can't be sold separately.

5. METHOD AND ROUTES OF ADMINISTRATION

Read the package leaflet before use.
Subcutaneous use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING, IF NECESSARY

The pen delivers 0.5 – 30 units in steps of 0.5 units.

If seal is broken before first use, contact pharmacist.

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator (2°C - 8°C).
Do not freeze. Do not expose to excessive heat or direct sunlight.
Once in use pens may be used for up to 28 days. . Discard after 28 days even if some of the solution remains. Pens in use should be stored below 30°C and should not be refrigerated.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Eli Lilly Nederland B.V.
Orteliuslaan 1000, 3528 BD Utrecht
The Netherlands

12. MARKETING AUTHORISATION NUMBER

EU/1/96/007/045

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Humalog 100 units/ml Junior KwikPen

17. UNIQUE IDENTIFIER – 2D BARCODE

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

LABEL TEXT

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE OF ADMINISTRATION

Humalog 100 units/ml Junior KwikPen solution for injection
insulin lispro
Subcutaneous use

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

3 ml

6. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON –Tempo Pen. Pack of 5

1. NAME OF THE MEDICINAL PRODUCT

Humalog 100 units/ml Tempo Pen solution for injection in a pre-filled pen.
insulin lispro

2. STATEMENT OF ACTIVE SUBSTANCE

One ml solution contains 100 units of insulin lispro (equivalent to 3.5mg).

3. LIST OF EXCIPIENTS

Excipients: glycerol, zinc oxide, dibasic sodium phosphate 7 H_20 with m-cresol as a preservative in water for injections. Sodium hydroxide and/or hydrochloric acid may have been used to adjust acidity. See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection.

5 pens of 3 ml

5. METHOD AND ROUTES OF ADMINISTRATION

Read the package leaflet before use.
Subcutaneous use

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children

7. OTHER SPECIAL WARNING, IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator (2°C - 8°C).
Do not freeze. Do not expose to excessive heat or direct sunlight.
Once in use pens may be used for up to 28 days. Pens in use should be stored below 30°C and should not be refrigerated.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Eli Lilly Nederland B.V.
Orteliuslaan 1000, 3528 BD Utrecht
The Netherlands

12. MARKETING AUTHORISATION NUMBER

EU/1/96/007/046

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

If seal is broken before first use, contact pharmacist.

16. INFORMATION IN BRAILLE

Humalog Tempo Pen

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON (with blue box) multipack – Tempo Pen

1. NAME OF THE MEDICINAL PRODUCT

Humalog 100 units/ml Tempo Pen solution for injection in a pre-filled pen
insulin lispro

2. STATEMENT OF ACTIVE SUBSTANCE

One ml solution contains 100 units of insulin lispro (equivalent to 3.5mg).

3. LIST OF EXCIPIENTS

Excipients: glycerol, zinc oxide, dibasic sodium phosphate 7 H_20 with m-cresol as a preservative in water for injections. Sodium hydroxide and/or hydrochloric acid may have been used to adjust acidity. See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection.

Multipack: 10 (2 packs of 5) pens of 3 ml.

5. METHOD AND ROUTES OF ADMINISTRATION

Read the package leaflet before use
Subcutaneous use

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children

7. OTHER SPECIAL WARNING, IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator (2°C - 8°C).
Do not freeze. Do not expose to excessive heat or direct sunlight.
Once in use pens may be used for up to 28 days. Pens in use should be stored below 30°C and should not be refrigerated.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Eli Lilly Nederland B.V.
Orteliuslaan 1000, 3528 BD Utrecht
The Netherlands

12. MARKETING AUTHORISATION NUMBER

EU/1/96/007/047

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Humalog Tempo Pen

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

INTERMEDIATE CARTON (without blue box) component of a multipack – Tempo Pen

1. NAME OF THE MEDICINAL PRODUCT

Humalog 100 units/ml Tempo Pen solution for injection in a pre-filled pen
insulin lispro

2. STATEMENT OF ACTIVE SUBSTANCE

One ml solution contains 100 units of insulin lispro (equivalent to 3.5mg).

3. LIST OF EXCIPIENTS

Excipients: glycerol, zinc oxide, dibasic sodium phosphate 7 H_20 with m-cresol as a preservative in water for injections. Sodium hydroxide and/or hydrochloric acid may have been used to adjust acidity. See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection.

5 pens of 3 ml. Component of a multipack, can't be sold separately.

5. METHOD AND ROUTES OF ADMINISTRATION

Read the package leaflet before use.
Subcutaneous use

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children

7. OTHER SPECIAL WARNING, IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator (2°C - 8°C).
Do not freeze. Do not expose to excessive heat or direct sunlight.
Once in use pens may be used for up to 28 days. Pens in use should be stored below 30°C and should not be refrigerated.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Eli Lilly Nederland B.V.
Orteliuslaan 1000, 3528 BD Utrecht
The Netherlands

12. MARKETING AUTHORISATION NUMBER

EU/1/96/007/047

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

If seal is broken before first use, contact pharmacist.

16. INFORMATION IN BRAILLE

Humalog Tempo Pen

17. UNIQUE IDENTIFIER – 2D BARCODE

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

LABEL TEXT

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE OF ADMINISTRATION

Humalog 100 units/ml Tempo Pen solution for injection
insulin lispro
Subcutaneous use

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

3 ml

6. OTHER

B. PACKAGE LEAFLET

Package leaflet: Information for the user

Humalog 100 units/ml solution for injection in vial
insulin lispro

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Humalog is and what it is used for
2. What you need to know before you use Humalog
3. How to use Humalog
4. Possible side effects
5. How to store Humalog
6. Contents of the pack and other information

1. What Humalog is and what it is used for

Humalog is used to treat diabetes. Humalog works more quickly than normal human insulin because the insulin molecule has been changed slightly.

You get diabetes if your pancreas does not make enough insulin to control the level of glucose in your blood. Humalog is a substitute for your own insulin and is used to control glucose in the long term. It works very quickly and lasts a shorter time than soluble insulin (2 to 5 hours). You should normally use Humalog within 15 minutes of a meal.

Your doctor may tell you to use Humalog as well as a longer-acting insulin. Each kind of insulin comes with another patient information leaflet to tell you about it. Do not change your insulin unless your doctor tells you to. Be very careful if you do change insulin.

Humalog is suitable for use in adults and children.

2. What you need to know before you use Humalog

Do NOT use Humalog
- if you think **hypoglycaemia** (low blood sugar) is starting. Further in this leaflet it tells you how to deal with mild hypoglycaemia (see Section 3: If you use more Humalog than you should).
- if you are **allergic** to insulin lispro or any of the other ingredients of this medicine (listed in section 6).

Warnings and precautions
- Always check the pack and the vial label for the name and type of the insulin when you get it from your pharmacy. Make sure you get the Humalog that your doctor has told you to use.
- **If your blood sugar levels are well controlled by your current insulin therapy, you may not feel the warning** symptoms when your blood sugar is falling too low. Warning signs are listed later in this leaflet. You must think carefully about when to have your meals, how often to exercise and how much to do. You must also keep a close watch on your blood sugar levels by testing your blood glucose often.

- A few people who have had hypoglycaemia after switching from animal insulin to human insulin have reported that the early warning symptoms were less obvious or different. If you often have hypoglycaemia or have difficulty recognising it, please discuss this with your doctor.
- If you answer YES to any of the following questions, tell your doctor, pharmacist or diabetes nurse
  - Have you recently become ill?
  - Do you have trouble with your kidneys or liver?
  - Are you exercising more than usual?
- The amount of insulin you need may also change if you drink alcohol.
- You should also tell your doctor, pharmacist or diabetes nurse if you are planning to go abroad. The time difference between countries may mean that you have to have your injections and meals at different times from when you are at home.
- Some patients with long-standing type 2 diabetes mellitus and heart disease or previous stroke who were treated with pioglitazone and insulin experienced the development of heart failure. Inform your doctor as soon as possible, if you experience signs of heart failure such as unusual shortness of breath or rapid increase in weight or localised swelling (oedema).

Skin changes at the injection site
The injection site should be rotated to prevent skin changes such as lumps under the skin. The insulin may not work very well if you inject into a lumpy area (See How to use Humalog). Contact your doctor if you are currently injecting into a lumpy area before you start injecting a different area. Your doctor may tell you to check your blood sugar more closely, and to adjust your insulin or your other antidiabetic medications dose.

Other medicines and Humalog
Your insulin needs may change if you are taking
- the contraceptive pill,
- steroids,
- thyroid hormone replacement therapy,
- oral hypoglycaemics,
- acetyl salicylic acid,
- sulpha antibiotics,
- octreotide,
- "beta$_2$ stimulants" (for example ritodrine, salbutamol or terbutaline),
- beta-blockers, or
- some antidepressants (monoamine oxidase inhibitors or selective serotonin reuptake inhibitors),
- danazol,
- some angiotensin converting enzyme (ACE) inhibitors (for example captopril, enalapril), and
- angiotensin II receptor blockers.

Please tell your doctor, if you are taking, have recently taken or might take any other medicines, including medicines obtained without a prescription (see section "Warnings and precautions").

Pregnancy and breast-feeding
Are you pregnant or thinking about becoming pregnant, or are you breast-feeding? The amount of insulin you need usually falls during the first three months of pregnancy and increases for the remaining six months. If you are breast-feeding, you may need to alter your insulin intake or diet. Ask your doctor for advice.

Driving and using machines
Your ability to concentrate and react may be reduced if you have hypoglycaemia. Please keep this possible problem in mind in all situations where you might put yourself and others at risk (e.g. driving a car or operating machinery). You should contact your doctor about the advisability of driving if you have:
- frequent episodes of hypoglycaemia

- reduced or absent warning signs of hypoglycaemia

Humalog contains sodium
This medicine contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially 'sodium-free'.

3. How to use Humalog

Always use Humalog exactly as your doctor has told you. You should check with your doctor if you are not sure.

Dose
- You should normally inject Humalog within 15 minutes of a meal. If you need to, you can inject soon after a meal. But your doctor will have told you exactly how much to use, when to use it, and how often. These instructions are only for you. Follow them exactly and visit your diabetes clinic regularly.
- If you change the type of insulin you use (for example from a human or animal insulin to a Humalog product), you may have to take more or less than before. This might just be for the first injection or it may be a gradual change over several weeks or months.
- Inject Humalog under the skin. You should only inject it into a muscle if your doctor has told you to.

Preparing Humalog
- Humalog is already dissolved in water, so you do not need to mix it. But you must use it **only** if it looks like water. It must be clear, have no colour and no solid pieces in it. Check each time you inject yourself.

Injecting Humalog
- First wash your hands.
- Before you make an injection, clean your skin as you have been instructed. Clean the rubber stopper on the vial, but do not remove the stopper.
- Use a clean, sterile syringe and needle to pierce the rubber stopper and draw in the amount of Humalog you want. Your doctor or clinic will tell you how to do this. **Do not share your needles and syringes.**
- Inject under the skin, as you were taught. Do not inject directly into a vein. After your injection, leave the needle in the skin for five seconds to make sure you have taken the whole dose. Do not rub the area you have just injected. Make sure you inject at least half an inch (1 cm) from the last injection and that you 'rotate' the places you inject, as you have been taught. It doesn't matter which injection site you use, either upper arm, thigh, buttock or abdomen, your Humalog injection will still work quicker than soluble human insulin.
- Your doctor will tell you if you have to mix Humalog with one of the human insulins. For example if you do need to inject a mixture, draw the Humalog into the syringe before the long acting insulin. Inject the liquid as soon as you have mixed it. Do the same thing every time. You should not normally mix Humalog with one of the mixtures of human insulins. You should never mix Humalog with insulins produced by other manufacturers or animal insulins.
- You must not administer Humalog by the intravenous route. Inject Humalog as your physician or nurse has taught you. Only your physician can administer Humalog by the intravenous route. He will only do this under special circumstances such as surgery or if you are ill and your glucose levels are too high.

Using Humalog in an infusion pump
- Only certain CE-marked insulin infusion pumps may be used to infuse insulin lispro. Before infusing insulin lispro, the manufacturers instructions should be studied to ascertain the suitability or otherwise for the particular pump. Read and follow the instructions in the product literature supplied with the infusion pump.

- Be sure to use the correct reservoir and catheter for your pump.
- Changing of the infusion set (tubing and needle) must be done according to the instructions in the product information supplied with the infusion set.
- In the event of a hypoglycaemic episode, the infusion should be stopped until the episode is resolved. If repeated or severe low blood glucose levels occur, notify your doctor or clinic and consider the need to reduce or stop your insulin infusion.
- A pump malfunction or obstruction of the infusion set can result in a rapid rise in glucose levels. If an interruption to insulin flow is suspected, follow the instructions in the product literature and if appropriate, notify your doctor or clinic.
- When used with an insulin infusion pump, Humalog should not be mixed with any other insulin.

If you use more Humalog than you should
If you use more Humalog than you need or are unsure how much you have injected, a low blood sugar may occur. Check your blood sugar.

If your blood sugar is low **(mild hypoglycaemia)**, eat glucose tablets, sugar or drink a sugary drink. Then eat fruit, biscuits, or a sandwich, as your doctor has advised you and have some rest. This will often get you over mild hypoglycaemia or a minor insulin overdose. If you get worse and your breathing is shallow and your skin gets pale, tell your doctor at once. A glucagon injection can treat quite severe hypoglycaemia. Eat glucose or sugar after the glucagon injection. If you do not respond to glucagon, you will have to go to hospital. Ask your doctor to tell you about glucagon.

If you forget to use Humalog
If you take less Humalog than you need or are unsure how much you have injected, a high blood sugar may occur. Check your blood sugar.

If hypoglycaemia (low blood sugar) or hyperglycaemia (high blood sugar) is not treated they can be very serious and cause headaches, nausea, vomiting, dehydration, unconsciousness, coma or even death (see A and B in section 4 “Possible Side Effects”).

Three simple steps to avoid hypoglycaemia or hyperglycaemia are:
- Always keep spare syringes and a spare vial of Humalog.
- Always carry something to show you are diabetic.
- Always carry sugar with you.

If you stop using Humalog.
If you take less Humalog than you need, a high blood sugar may occur. Do not change your insulin unless your doctor tells you to.

If you have any further questions on the use of this product, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Systemic allergy is rare (≥ 1/10,000 to <1/1,000). The symptoms are as follows:
- rash over the whole body
- difficulty in breathing
- wheezing
- blood pressure dropping
- heart beating fast
- sweating.

If you think you are having this sort of insulin allergy with Humalog, tell your doctor at once.

Local allergy is common (≥ 1/100 to <1/10). Some people get redness, swelling or itching around the area of the insulin injection. This usually clears up in anything from a few days to a few weeks. If this happens to you, tell your doctor.

Lipodystrophy is uncommon (≥ 1/1,000 to <1/100). If you inject insulin too often at the same place, the fatty tissue may either shrink (lipoatrophy) or thicken (lipohypertrophy). Lumps under the skin may also be caused by build-up of a protein called amyloid (cutaneous amyloidosis). The insulin may not work very well if you inject into a lumpy area. Change the injection site with each injection to help prevent these skin changes.

Oedema (e.g. swelling in arms, ankles; fluid retention) has been reported, particularly at the start of insulin therapy or during a change in therapy to improve control of your blood glucose.

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

Common problems of diabetes

A. Hypoglycaemia
Hypoglycaemia (low blood sugar) means there is not enough sugar in the blood. This can be caused if:
- you take too much Humalog or other insulin;
- you miss or delay meals or change your diet;
- you exercise or work too hard just before or after a meal;
- you have an infection or illness (especially diarrhoea or vomiting);
- there is a change in your need for insulin; or
- you have trouble with your kidneys or liver which gets worse.

Alcohol and some medicines can affect your blood sugar levels.

The first symptoms of low blood sugar usually come on quickly and include the following:
- tiredness
- nervousness or shakiness
- headache
- rapid heartbeat
- feeling sick
- cold sweat.

While you are not confident about recognising your warning symptoms, avoid situations, e.g. driving a car, in which you or others would be put at risk by hypoglycaemia.

B. Hyperglycaemia and diabetic ketoacidosis
Hyperglycaemia (too much sugar in the blood) means that your body does not have enough insulin. Hyperglycaemia can be brought about by:
- not taking your Humalog or other insulin;
- taking less insulin than your doctor tells you to;
- eating a lot more than your diet allows; or
- fever, infection or emotional stress.

Hyperglycaemia can lead to diabetic ketoacidosis. The first symptoms come on slowly over many hours or days. The symptoms include the following:
- feeling sleepy
- flushed face
- thirst
- no appetite
- fruity smell on the breath
- feeling or being sick

Severe symptoms are heavy breathing and a rapid pulse. **Get medical help immediately.**

C. Illness
If you are ill, especially if you feel sick or are sick, the amount of insulin you need may change. **Even when you are not eating normally, you still need insulin.** Test your urine or blood, follow your 'sick rules', and tell your doctor.

5. How to store Humalog

Before the first use store your Humalog in a refrigerator (2°C – 8°C). Do not freeze. Keep your vial in use in a refrigerator (2°C – 8°C) or at room temperature (below 30°C) and discard after 28 days. Do not put it near heat or in the sun.

Keep out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the label and the carton. The expiry date refers to the last day of that month.

Do not use this medicine if you notice it is coloured or it has solid pieces in it. You must use it **only** if it looks like water. Check this each time you inject yourself.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. Contents of the pack and other information

What Humalog 100 units/ml solution for injection in vial contains
- The active substance is insulin lispro. Insulin lispro is made in the laboratory by a 'recombinant DNA technology' process. It is a changed form of human insulin and so is different from other human and animal insulins. Insulin lispro is closely related to human insulin which is a natural hormone made by the pancreas.
- The other ingredients are m-cresol, glycerol, dibasic sodium phosphate 7 H_2O, zinc oxide and water for injection. Sodium hydroxide or hydrochloric acid may have been used to adjust the acidity.

What Humalog looks like and contents of the pack
Humalog 100 units/ml solution for injection is a sterile, clear, colourless, aqueous solution and contains 100 units of insulin lispro in each millilitre (100 units/ml) solution for injection. Each vial contains 1000 units (10 millilitres). Humalog 100 units/ml solution for injection in vial comes in a pack of 1 vial, 2 vials or a multipack of 5 x 1 vial. Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer
Humalog 100 units/ml solution for injection in vial is made by:
- Lilly S.A., Avda. de la Industria 30, 28108 Alcobendas, Madrid, Spain.

The product licence is held by: Eli Lilly Nederland B.V., Orteliuslaan 1000, 3528 BD Utrecht, The Netherlands.

For any information about this medicinal product, please contact the local representative of the Marketing Authorisation Holder:

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This leaflet was last revised in {MM/YYYY}.

Detailed information on this medicine is available on the European Medicines Agency web site: https://www.ema.europa.eu.

Package leaflet: Information for the user

Humalog 100 units/ml solution for injection in cartridge
insulin lispro

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Humalog is and what it is used for
2. What you need to know before you use Humalog
3. How to use Humalog
4. Possible side effects
5. How to store Humalog
6. Contents of the pack and other information

1. What Humalog is and what it is used for

Humalog is used to treat diabetes. Humalog works more quickly than normal human insulin because the insulin molecule has been changed slightly.

You get diabetes if your pancreas does not make enough insulin to control the level of glucose in your blood. Humalog is a substitute for your own insulin and is used to control glucose in the long term. It works very quickly and lasts a shorter time than soluble insulin (2 to 5 hours). You should normally use Humalog within 15 minutes of a meal.

Your doctor may tell you to use Humalog as well as a longer-acting insulin. Each kind of insulin comes with another patient information leaflet to tell you about it. Do not change your insulin unless your doctor tells you to. Be very careful if you do change insulin.

Humalog is suitable for use in adults and children.

2. What you need to know before you use Humalog

Do NOT use Humalog
- if you think **hypoglycaemia** (low blood sugar) is starting. Further in this leaflet it tells you how to deal with mild hypoglycaemia (see Section 3: If you use more Humalog than you should).
- if you are **allergic** to insulin lispro or any of the other ingredients of this medicine (listed in section 6).

Warnings and precautions
- Always check the pack and the cartridge label for the name and type of the insulin when you get it from your pharmacy. Make sure you get the Humalog that your doctor has told you to use.
- If your blood sugar levels are well controlled by your current insulin therapy, you may not feel the warning symptoms when your blood sugar is falling too low. Warning signs are listed later in this leaflet. You must think carefully about when to have your meals, how often to exercise and how much to do. You must also keep a close watch on your blood sugar levels by testing your blood glucose often.

- A few people who have had hypoglycaemia after switching from animal insulin to human insulin have reported that the early warning symptoms were less obvious or different. If you often have hypoglycaemia or have difficulty recognising it, please discuss this with your doctor.
- If you answer YES to any of the following questions, tell your doctor, pharmacist or diabetes nurse
  - Have you recently become ill?
  - Do you have trouble with your kidneys or liver?
  - Are you exercising more than usual?
- The amount of insulin you need may also change if you drink alcohol.
- You should also tell your doctor, pharmacist or diabetes nurse if you are planning to go abroad. The time difference between countries may mean that you have to have your injections and meals at different times from when you are at home.
- Some patients with long-standing type 2 diabetes mellitus and heart disease or previous stroke who were treated with pioglitazone and insulin experienced the development of heart failure. Inform your doctor as soon as possible, if you experience signs of heart failure such as unusual shortness of breath or rapid increase in weight or localised swelling (oedema).

Skin changes at the injection site
The injection site should be rotated to prevent skin changes such as lumps under the skin. The insulin may not work very well if you inject into a lumpy area (See How to use Humalog). Contact your doctor if you are currently injecting into a lumpy area before you start injecting a different area. Your doctor may tell you to check your blood sugar more closely, and to adjust your insulin or your other antidiabetic medications dose.

Other medicines and Humalog
Your insulin needs may change if you are taking
- the contraceptive pill,
- steroids,
- thyroid hormone replacement therapy,
- oral hypoglycaemics,
- acetyl salicylic acid,
- sulpha antibiotics,
- octreotide,
- "beta$_2$ stimulants" (for example ritodrine, salbutamol or terbutaline),
- beta-blockers, or
- some antidepressants (monoamine oxidase inhibitors or selective serotonin reuptake inhibitors),
- danazol,
- some angiotensin converting enzyme (ACE) inhibitors (for example captopril, enalapril), and
- angiotensin II receptor blockers.

Please tell your doctor, if you are taking, have recently taken or might take any other medicines, including medicines obtained without a prescription (see section "Warnings and precautions").

Pregnancy and breast-feeding
Are you pregnant or thinking about becoming pregnant, or are you breast-feeding? The amount of insulin you need usually falls during the first three months of pregnancy and increases for the remaining six months. If you are breast-feeding, you may need to alter your insulin intake or diet. Ask your doctor for advice.

Driving and using machines
Your ability to concentrate and react may be reduced if you have hypoglycaemia. Please keep this possible problem in mind in all situations where you might put yourself and others at risk (e.g. driving a car or operating machinery). You should contact your doctor about the advisability of driving if you have:
- frequent episodes of hypoglycaemia

- reduced or absent warning signs of hypoglycaemia

Humalog contains sodium
This medicine contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially 'sodium-free'.

3. How to use Humalog

The 3 ml cartridge is only for use in Lilly 3 ml pens. It is not for use in 1.5 ml pens.

Always use Humalog exactly as your doctor has told you. You should check with your doctor if you are not sure. To prevent the possible transmission of disease, each cartridge must be used by you only, even if the needle on the delivery device is changed.

Dose
- You should normally inject Humalog within 15 minutes of a meal. If you need to, you can inject soon after a meal. But your doctor will have told you exactly how much to use, when to use it, and how often. These instructions are only for you. Follow them exactly and visit your diabetes clinic regularly.
- If you change the type of insulin you use (for example from a human or animal insulin to a Humalog product), you may have to take more or less than before. This might just be for the first injection or it may be a gradual change over several weeks or months.
- Inject Humalog under the skin. You should only inject it into a muscle if your doctor has told you to.

Preparing Humalog
- Humalog is already dissolved in water, so you do not need to mix it. But you must use it **only** if it looks like water. It must be clear, have no colour and no solid pieces in it. Check each time you inject yourself.

Getting the pen ready to use
- First wash your hands. Disinfect the rubber membrane of the cartridge.
- **You must only use Humalog cartridges in Lilly insulin pens. Please make sure that Humalog or Lilly cartridges are mentioned in the leaflet accompanying your pen. The 3 ml cartridge only fits the 3 ml pen.**
- Follow the instructions that come with the pen. Put the cartridge into the pen.
- You will set the dose to 1 or 2 units. Then hold the pen with the needle pointing up and tap the side of the pen so that any bubbles float to the top. With the pen still pointing up, press the injection mechanism. Do this until a drop of Humalog comes out of the needle. There may still be some small air bubbles left in the pen. These are harmless, but if the air bubble is too big, it may make the dose of your injection less accurate.

Injecting Humalog
- Before you make an injection, clean your skin as you have been instructed. Inject under the skin, as you were taught. Do not inject directly into a vein. After your injection, leave the needle in the skin for five seconds to make sure you have taken the whole dose. Do not rub the area you have just injected. Make sure you inject at least half an inch (1 cm) from the last injection and that you 'rotate' the places you inject, as you have been taught. It doesn't matter which injection site you use, either upper arm, thigh, buttock or abdomen, your Humalog injection will still work quicker than soluble human insulin.
- You must not administer Humalog by the intravenous route. Inject Humalog as your physician or nurse has taught you. Only your physician can administer Humalog by the intravenous route. He will only do this under special circumstances such as surgery or if you are ill and your glucose levels are too high.

After injecting

- As soon as you have done the injection, take the needle off the pen using the outer needle cap. This will keep the Humalog sterile and prevent leaking. It will also stop air going back into the pen and the needle clogging up. **Do not share your needles.** Do not share your pen. Replace the cap on your pen. Leave the cartridge in the pen.

Further injections

- Before every injection, dial 1 or 2 units and press the injection mechanism with the pen pointing up until a drop of Humalog comes out of the needle. You can see how much Humalog is left by looking at the gauge on the side of the cartridge. The distance between each mark on the gauge is about 20 units. If there is not enough for your dose, change the cartridge.

Do not mix any other insulin in a Humalog cartridge. Once the cartridge is empty, do not use it again.

Using Humalog in an infusion pump

- Only certain CE-marked insulin infusion pumps may be used to infuse insulin lispro. Before infusing insulin lispro, the manufacturers instructions should be studied to ascertain the suitability or otherwise for the particular pump. Read and follow the instructions in the product literature supplied with the infusion pump.
- Be sure to use the correct reservoir and catheter for your pump.
- Changing of the infusion set (tubing and needle) must be done according to the instructions in the product information supplied with the infusion set.
- In the event of a hypoglycaemic episode, the infusion should be stopped until the episode is resolved. If repeated or severe low blood glucose levels occur, notify your doctor or clinic and consider the need to reduce or stop your insulin infusion.
- A pump malfunction or obstruction of the infusion set can result in a rapid rise in glucose levels. If an interruption to insulin flow is suspected, follow the instructions in the product literature and if appropriate, notify your doctor or clinic.
- When used with an insulin infusion pump, Humalog should not be mixed with any other insulin.

If you use more Humalog than you should

If you use more Humalog than you need or are unsure how much you have injected, a low blood sugar may occur. Check your blood sugar.

If your blood sugar is low **(mild hypoglycaemia)**, eat glucose tablets, sugar or drink a sugary drink. Then eat fruit, biscuits, or a sandwich, as your doctor has advised you and have some rest. This will often get you over mild hypoglycaemia or a minor insulin overdose. If you get worse and your breathing is shallow and your skin gets pale, tell your doctor at once. A glucagon injection can treat quite severe hypoglycaemia. Eat glucose or sugar after the glucagon injection. If you do not respond to glucagon, you will have to go to hospital. Ask your doctor to tell you about glucagon.

If you forget to use Humalog

If you take less Humalog than you need or are unsure how much you have injected, a high blood sugar may occur. Check your blood sugar

If hypoglycaemia (low blood sugar) or hyperglycaemia (high blood sugar) is not treated they can be very serious and cause headaches, nausea, vomiting, dehydration, unconsciousness, coma or even death (see A and B in section 4 “Possible Side Effects”).

Three simple steps to avoid hypoglycaemia or hyperglycaemia are:

- Always keep spare syringes and a spare vial of Humalog, or a spare pen and cartridges, in case you lose your pen or cartridges or they get damaged.
- Always carry something to show you are diabetic.
- Always carry sugar with you.

If you stop using Humalog.
If you take less Humalog than you need, a high blood sugar may occur. Do not change your insulin unless your doctor tells you to.

If you have any further questions on the use of this product, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Systemic allergy is rare (≥ 1/10,000 to <1/1,000). The symptoms are as follows:
- rash over the whole body
- difficulty in breathing
- wheezing
- blood pressure dropping
- heart beating fast
- sweating

If you think you are having this sort of insulin allergy with Humalog, tell your doctor at once.

Local allergy is common (≥ 1/100 to <1/10). Some people get redness, swelling or itching around the area of the insulin injection. This usually clears up in anything from a few days to a few weeks. If this happens to you, tell your doctor.

Lipodystrophy is uncommon (≥ 1/1,000 to <1/100). If you inject insulin too often at the same place, the fatty tissue may either shrink (lipoatrophy) or thicken (lipohypertrophy). Lumps under the skin may also be caused by build-up of a protein called amyloid (cutaneous amyloidosis). The insulin may not work very well if you inject into a lumpy area. Change the injection site with each injection to help prevent these skin changes.

Oedema (e.g. swelling in arms, ankles; fluid retention) has been reported, particularly at the start of insulin therapy or during a change in therapy to improve control of your blood glucose.

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

Common problems of diabetes

A. Hypoglycaemia
Hypoglycaemia (low blood sugar) means there is not enough sugar in the blood. This can be caused if:
- you take too much Humalog or other insulin;
- you miss or delay meals or change your diet;
- you exercise or work too hard just before or after a meal;
- you have an infection or illness (especially diarrhoea or vomiting);
- there is a change in your need for insulin; or
- you have trouble with your kidneys or liver which gets worse.

Alcohol and some medicines can affect your blood sugar levels.

The first symptoms of low blood sugar usually come on quickly and include the following:
- tiredness
- nervousness or shakiness
- headache
- rapid heartbeat
- feeling sick
- cold sweat.

While you are not confident about recognising your warning symptoms, avoid situations, e.g. driving a car, in which you or others would be put at risk by hypoglycaemia.

B. Hyperglycaemia and diabetic ketoacidosis

Hyperglycaemia (too much sugar in the blood) means that your body does not have enough insulin. Hyperglycaemia can be brought about by:

- not taking your Humalog or other insulin;
- taking less insulin than your doctor tells you to;
- eating a lot more than your diet allows; or
- fever, infection or emotional stress.

Hyperglycaemia can lead to diabetic ketoacidosis. The first symptoms come on slowly over many hours or days. The symptoms include the following:

- feeling sleepy
- flushed face
- thirst
- no appetite
- fruity smell on the breath
- feeling or being sick.

Severe symptoms are heavy breathing and a rapid pulse. **Get medical help immediately.**

C. Illness

If you are ill, especially if you feel sick or are sick, the amount of insulin you need may change. **Even when you are not eating normally, you still need insulin.** Test your urine or blood, follow your 'sick rules', and tell your doctor.

5. How to store Humalog

Before the first use store your Humalog in a refrigerator (2°C – 8°C). Do not freeze.

Keep your cartridge in use at room temperature (below 30°C) and discard after 28 days. Do not put it near heat or in the sun. Do not keep your pen or the cartridges you are using in the fridge. The pen with the inserted cartridge should not be stored with the needle attached.

Keep out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the label and the carton. The expiry date refers to the last day of that month.

Do not use this medicine if you notice it is coloured or it has solid pieces in it. You must use it **only** if it looks like water. Check this each time you inject yourself.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. Contents of the pack and other information

What Humalog 100 units/ml solution for injection in cartridge contains

- The active substance is insulin lispro. Insulin lispro is made in the laboratory by a 'recombinant DNA technology' process. It is a changed form of human insulin and so is different from other human and animal insulins. Insulin lispro is closely related to human insulin which is a natural hormone made by the pancreas.
- The other ingredients are m-cresol, glycerol, dibasic sodium phosphate 7 H_2O, zinc oxide and water for injection. Sodium hydroxide or hydrochloric acid may have been used to adjust the acidity.

What Humalog looks like and contents of the pack

Humalog 100 units/ml solution for injection is a sterile, clear, colourless, aqueous solution and contains 100 units of insulin lispro in each millilitre (100 units/ml) solution for injection. Each

cartridge contains 300 units (3 millilitres). The cartridges come in packs of 5 or10 cartridges. Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer
Humalog 100 units/ml solution for injection in cartridge is made by:

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- Eli Lilly Italia S.p.A., Via Gramsci 731-733, 50019 Sesto Fiorentino, (FI) Italy.

The product licence is held by: Eli Lilly Nederland B.V., Orteliuslaan 1000, 3528 BD Utrecht, The Netherlands.

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This leaflet was last revised in {MM/YYYY}.

Detailed information on this medicine is available on the European Medicines Agency web site: https://www.ema.europa.eu.

Package leaflet: Information for the user

Humalog Mix25 100 units/ml suspension for injection in vial
insulin lispro

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Humalog Mix25 is and what it is used for
2. What you need to know before you use Humalog Mix25
3. How to use Humalog Mix25
4. Possible side effects
5. How to store Humalog Mix25
6. Contents of the pack and other information

1. What Humalog Mix25 is and what it is used for

Humalog Mix25 is used to treat diabetes. Humalog Mix25 is a premixed suspension. Its active substance is insulin lispro. 25% of the insulin lispro in Humalog Mix25 is dissolved in water and it works more quickly than normal human insulin because the insulin molecule has been changed slightly. 75% of the insulin lispro in Humalog Mix25 is available in a suspension together with protamine sulphate, so that its action is prolonged.

You get diabetes if your pancreas does not make enough insulin to control the level of glucose in your blood. Humalog Mix25 is a substitute for your own insulin and is used to control glucose in the long term. Humalog Mix25 works very quickly and longer than soluble insulin. You should normally use Humalog Mix25 within 15 minutes of a meal.

Your doctor may tell you to use Humalog Mix25 as well as a longer-acting insulin. Each kind of insulin comes with another patient information leaflet to tell you about it. Do not change your insulin unless your doctor tells you to. Be very careful if you do change insulin.

2. What you need to know before you use Humalog Mix25

Do NOT use Humalog Mix25
- if you think **hypoglycaemia** (low blood sugar) is starting. Further in this leaflet it tells you how to deal with mild hypoglycaemia (see Section 3: If you take more Humalog Mix25than you need).
- if you are **allergic** to insulin lispro or any of the other ingredients of this medicine (listed in section 6).

Warnings and precautions
- Always check the pack and the vial label for the name and type of the insulin when you get it from your pharmacy. Make sure you get the Humalog Mix25 that your doctor has told you to use.
- If your blood sugar levels are well controlled by your current insulin therapy, you may not feel the warning symptoms when your blood sugar is falling too low. Warning signs are listed later in this leaflet. You must think carefully about when to have your meals, how often to exercise and how much to do. You must also keep a close watch on your blood sugar levels by testing your blood glucose often.

- A few people who have had hypoglycaemia after switching from animal insulin to human insulin have reported that the early warning symptoms were less obvious or different. If you often have hypoglycaemia or have difficulty recognising them, please discuss this with your doctor.
- If you answer YES to any of the following questions, tell your doctor, pharmacist or diabetes nurse
  - Have you recently become ill?
  - Do you have trouble with your kidneys or liver?
  - Are you exercising more than usual?
- The amount of insulin you need may also change if you drink alcohol.
- You should also tell your doctor, pharmacist or diabetes nurse if you are planning to go abroad. The time difference between countries may mean that you have to have your injections and meals at different times from when you are at home.
- Some patients with long-standing type 2 diabetes mellitus and heart disease or previous stroke who were treated with pioglitazone and insulin experienced the development of heart failure. Inform your doctor as soon as possible, if you experience signs of heart failure such as unusual shortness of breath or rapid increase in weight or localised swelling (oedema).

Skin changes at the injection site
The injection site should be rotated to prevent skin changes such as lumps under the skin. The insulin may not work very well if you inject into a lumpy area (See How to use Humalog Mix25). Contact your doctor if you are currently injecting into a lumpy area before you start injecting a different area. Your doctor may tell you to check your blood sugar more closely, and to adjust your insulin or your other antidiabetic medications dose.

Other medicines and Humalog Mix25
Your insulin needs may change if you are taking
- the contraceptive pill,
- steroids,
- thyroid hormone replacement therapy,
- oral hypoglycaemics,
- acetyl salicylic acid,
- sulpha antibiotics,
- octreotide,
- "beta$_2$ stimulants" (for example ritodrine, salbutamol or terbutaline),
- beta-blockers, or
- some antidepressants (monoamine oxidase inhibitors or selective serotonin reuptake inhibitors),
- danazol,
- some angiotensin converting enzyme (ACE) inhibitors (for example captopril, enalapril), and
- angiotensin II receptor blockers.

Please tell your doctor, if you are taking, have recently taken or might take any other medicines, including medicines obtained without a prescription (see section "Warnings and precautions").

Pregnancy and breast-feeding
Are you pregnant or thinking about becoming pregnant, or are you breast-feeding? The amount of insulin you need usually falls during the first three months of pregnancy and increases for the remaining six months. If you are breast-feeding, you may need to alter your insulin intake or diet. Ask your doctor for advice.

Driving and using machines
Your ability to concentrate and react may be reduced if you have hypoglycaemia. Please keep this possible problem in mind in all situations where you might put yourself and others at risk (e.g. driving a car or operating machinery). You should contact your doctor about the advisability of driving if you have:
- frequent episodes of hypoglycaemia

- reduced or absent warning signs of hypoglycaemia

Humalog Mix25 contains sodium
This medicine contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially 'sodium-free'.

3. How to use Humalog Mix25

Always use Humalog Mix25 exactly as your doctor has told you. You should check with your doctor if you are not sure.

Dose
- You should normally inject Humalog Mix25 within 15 minutes of a meal. If you need to, you can inject soon after a meal. But your doctor will have told you exactly how much to use, when to use it, and how often. These instructions are only for you. Follow them exactly and visit your diabetes clinic regularly.
- If you change the type of insulin you use (for example from a human or animal insulin to a Humalog product), you may have to take more or less than before. This might just be for the first injection or it may be a gradual change over several weeks or months.
- Inject Humalog Mix25 under the skin. You should not administer it using a different administration route. Under no circumstances should Humalog Mix25 be given intravenously.

Preparing Humalog Mix25
- Vials containing Humalog Mix25 should be rotated in the palms of the hands before use to resuspend insulin until it appears uniformly cloudy or milky. Do not shake vigorously as this may cause frothing which may interfere with the correct measurement of the dose. The vials should be examined frequently and should not be used if clumps of material are present or if solid white particles stick to the bottom or wall of the vial, giving it a frosted appearance. Check each time you inject yourself.

Injecting Humalog Mix25
- First wash your hands.
- Before you make an injection, clean your skin as you have been instructed. Clean the rubber stopper on the vial, but do not remove the stopper.
- Use a clean, sterile syringe and needle to pierce the rubber stopper and draw in the amount of Humalog Mix25 you want. Your doctor or clinic will tell you how to do this. **Do not share your needles and syringes.**
- Inject under the skin, as you were taught. Do not inject directly into a vein. After your injection, leave the needle in the skin for five seconds to make sure you have taken the whole dose. Do not rub the area you have just injected. Make sure you inject at least half an inch (1 cm) from the last injection and that you 'rotate' the places you inject, as you have been taught.

If you use more Humalog Mix25 than you need
If you use more Humalog Mix25 than you need or are unsure how much you have injected, a low blood sugar may occur. Check your blood sugar.

If your blood sugar is low **(mild hypoglycaemia)**, eat glucose tablets, sugar or drink a sugary drink. Then eat fruit, biscuits, or a sandwich, as your doctor has advised you and have some rest. This will often get you over mild hypoglycaemia or a minor insulin overdose. If you get worse and your breathing is shallow and your skin gets pale, tell your doctor at once. A glucagon injection can treat quite severe hypoglycaemia. Eat glucose or sugar after the glucagon injection. If you do not respond to glucagon, you will have to go to hospital. Ask your doctor to tell you about glucagon.

If you forget to use Humalog Mix25
If you take less Humalog Mix25 than you need or are unsure how much you have injected, a high blood sugar may occur. Check your blood sugar

If hypoglycaemia (low blood sugar) or hyperglycaemia (high blood sugar) is not treated they can be very serious and cause headaches, nausea, vomiting, dehydration, unconsciousness, coma or even death (see A and B in section 4 “Possible Side Effects”).

Three simple steps to avoid hypoglycaemia or hyperglycaemia are:
- Always keep spare syringes and a spare vial of Humalog Mix25.
- Always carry something to show you are diabetic.
- Always carry sugar with you.

If you stop using Humalog Mix25.
If you take less Humalog Mix25 than you need, a high blood sugar may occur. Do not change your insulin unless your doctor tells you to.

If you have any further questions on the use of this product, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Systemic allergy is rare (≥ 1/10,000 to <1/1,000). The symptoms are as follows:
- rash over the whole body
- difficulty in breathing
- wheezing
- blood pressure dropping
- heart beating fast
- sweating

If you think you are having this sort of insulin allergy with Humalog Mix25, tell your doctor at once.

Local allergy is common (≥ 1/100 to <1/10). Some people get redness, swelling or itching around the area of the insulin injection. This usually clears up in anything from a few days to a few weeks. If this happens to you, tell your doctor.

Lipodystrophy is uncommon (≥ 1/1,000 to <1/100). If you inject insulin too often at the same place, the fatty tissue may either shrink (lipoatrophy) or thicken (lipohypertrophy). Lumps under the skin may also be caused by build-up of a protein called amyloid (cutaneous amyloidosis). The insulin may not work very well if you inject into a lumpy area. Change the injection site with each injection to help prevent these skin changes.

Oedema (e.g. swelling in arms, ankles; fluid retention) has been reported, particularly at the start of insulin therapy or during a change in therapy to improve control of your blood glucose.

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

Common problems of diabetes

A. Hypoglycaemia
Hypoglycaemia (low blood sugar) means there is not enough sugar in the blood. This can be caused if:
- you take too much Humalog Mix25 or other insulin;
- you miss or delay meals or change your diet;
- you exercise or work too hard just before or after a meal;
- you have an infection or illness (especially diarrhoea or vomiting);
- there is a change in your need for insulin; or
- you have trouble with your kidneys or liver which gets worse.

Alcohol and some medicines can affect your blood sugar levels.

The first symptoms of low blood sugar usually come on quickly and include the following:
- tiredness
- nervousness or shakiness
- headache
- rapid heartbeat
- feeling sick
- cold sweat

While you are not confident about recognising your warning symptoms, avoid situations, e.g. driving a car, in which you or others would be put at risk by hypoglycaemia.

B. Hyperglycaemia and diabetic ketoacidosis

Hyperglycaemia (too much sugar in the blood) means that your body does not have enough insulin. Hyperglycaemia can be brought about by:
- not taking your Humalog or other insulin;
- taking less insulin than your doctor tells you to;
- eating a lot more than your diet allows; or
- fever, infection or emotional stress.

Hyperglycaemia can lead to diabetic ketoacidosis. The first symptoms come on slowly over many hours or days. The symptoms include the following:
- feeling sleepy
- flushed face
- thirst
- no appetite
- fruity smell on the breath
- feeling or being sick

Severe symptoms are heavy breathing and a rapid pulse. **Get medical help immediately.**

C. Illness

If you are ill, especially if you feel sick or are sick, the amount of insulin you need may change. **Even when you are not eating normally, you still need insulin.** Test your urine or blood, follow your 'sick rules', and tell your doctor.

5. How to store Humalog Mix25

Before the first use store your Humalog Mix25 in a refrigerator (2°C – 8°C). Do not freeze. Keep your vial in use in a refrigerator (2°C – 8°C) or at room temperature (below 30°C) and discard after 28 days. Do not put it near heat or in the sun.

Keep out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the label and the carton. The expiry date refers to the last day of that month.

Do not use this medicine if you notice clumps of material are present or if solid white particles stick to the bottom or wall of the vial, giving it a frosted appearance. Check each time you inject yourself.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. Contents of the pack and other information

What Humalog Mix25 100 units/ml suspension for injection in vial contains
- The active substance is insulin lispro. Insulin lispro is made in the laboratory by a 'recombinant DNA technology' process. It is a changed form of human insulin and so is different from other

human and animal insulins. Insulin lispro is closely related to human insulin which is a natural hormone made by the pancreas.
- The other ingredients are protamine sulphate, m-cresol, phenol, glycerol, dibasic sodium phosphate $7H_2O$, zinc oxide and water for injection. Sodium hydroxide or hydrochloric acid may have been used to adjust the acidity.

What Humalog Mix25 100 units/ml suspension for injection in vial looks like and contents of the pack
Humalog Mix25 100 units/ml suspension for injection is a white, sterile suspension and contains 100 units of insulin lispro in each millilitre (100 units/ml) suspension for injection. 25% of the insulin lispro in Humalog Mix25 is dissolved in water. 75% of the insulin lispro in Humalog Mix25 is available in a suspension together with protamine sulphate. Each vial contains 1000 units (10 millilitres). Humalog Mix25 100 units/ml suspension for injection in vial comes in a pack of 1 vial.

Marketing Authorisation Holder and Manufacturer
Humalog Mix25 100 units/ml suspension for injection in vial is made by:
- Lilly S.A., Avda. de la Industria 30, 28108 Alcobendas, Madrid, Spain.

The product licence is held by: Eli Lilly Nederland B.V., Orteliuslaan 1000, 3528 BD Utrecht, The Netherlands.

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Detailed information on this medicine is available on the European Medicines Agency web site: https://www.ema.europa.eu.

Package leaflet: Information for the user

Humalog Mix25 100 units/ml suspension for injection in cartridge
insulin lispro

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Humalog Mix25 is and what it is used for
2. What you need to know before you use Humalog Mix25
3. How to use Humalog Mix25
4. Possible side effects
5. How to store Humalog Mix25
6. Contents of the pack and other information

1. What Humalog Mix25 is and what it is used for

Humalog Mix25 is used to treat diabetes. Humalog Mix25 is a premixed suspension. Its active substance is insulin lispro. 25% of the insulin lispro in Humalog Mix25 is dissolved in water and it works more quickly than normal human insulin because the insulin molecule has been changed slightly. 75% of the insulin lispro in Humalog Mix25 is available in a suspension together with protamine sulphate, so that its action is prolonged.

You get diabetes if your pancreas does not make enough insulin to control the level of glucose in your blood. Humalog Mix25 is a substitute for your own insulin and is used to control glucose in the long term. Humalog Mix25 works very quickly and longer than soluble insulin. You should normally use Humalog Mix25 within 15 minutes of a meal.

Your doctor may tell you to use Humalog Mix25 as well as a longer-acting insulin. Each kind of insulin comes with another patient information leaflet to tell you about it. Do not change your insulin unless your doctor tells you to. Be very careful if you do change insulin.

2. What you need to know before you use Humalog Mix25

Do NOT use Humalog Mix25
- if you think **hypoglycaemia** (low blood sugar) is starting. Further in this leaflet it tells you how to deal with mild hypoglycaemia (see Section 3: If you take more Humalog Mix25 than you need).
- if you are **allergic** to insulin lispro or any of the other ingredients of this medicine (listed in section 6).

Warnings and precautions
- Always check the pack and the cartridge label for the name and type of the insulin when you get it from your pharmacy. Make sure you get the Humalog Mix25 that your doctor has told you to use.
- If your blood sugar levels are well controlled by your current insulin therapy, you may not feel the warning symptoms when your blood sugar is falling too low. Warning signs are listed later in this leaflet. You must think carefully about when to have your meals, how often to exercise and how

much to do. You must also keep a close watch on your blood sugar levels by testing your blood glucose often.
- A few people who have had hypoglycaemia after switching from animal insulin to human insulin have reported that the early warning symptoms were less obvious or different. If you often have hypoglycaemia or have difficulty recognising them, please discuss this with your doctor.
- If you answer YES to any of the following questions, tell your doctor, pharmacist or diabetes nurse
  - Have you recently become ill?
  - Do you have trouble with your kidneys or liver?
  - Are you exercising more than usual?
- The amount of insulin you need may also change if you drink alcohol.
- You should also tell your doctor, pharmacist or diabetes nurse if you are planning to go abroad. The time difference between countries may mean that you have to have your injections and meals at different times from when you are at home.
- Some patients with long-standing type 2 diabetes mellitus and heart disease or previous stroke who were treated with pioglitazone and insulin experienced the development of heart failure. Inform your doctor as soon as possible, if you experience signs of heart failure such as unusual shortness of breath or rapid increase in weight or localised swelling (oedema).

Skin changes at the injection site
The injection site should be rotated to prevent skin changes such as lumps under the skin. The insulin may not work very well if you inject into a lumpy area (See How to use Humalog Mix25). Contact your doctor if you are currently injecting into a lumpy area before you start injecting a different area. Your doctor may tell you to check your blood sugar more closely, and to adjust your insulin or your other antidiabetic medications dose.

Other medicines and Humalog Mix25
Your insulin needs may change if you are taking
- the contraceptive pill,
- steroids,
- thyroid hormone replacement therapy,
- oral hypoglycaemics,
- acetyl salicylic acid,
- sulpha antibiotics,
- octreotide,
- "beta$_2$ stimulants" (for example ritodrine, salbutamol or terbutaline),
- beta-blockers, or
- some antidepressants (monoamine oxidase inhibitors or selective serotonin reuptake inhibitors),
- danazol,
- some angiotensin converting enzyme (ACE) inhibitors (for example captopril, enalapril), and
- angiotensin II receptor blockers.

Please tell your doctor, if you are taking, have recently taken or might take any other medicines, including medicines obtained without a prescription (see section "Warnings and precautions").

Pregnancy and breast-feeding
Are you pregnant or thinking about becoming pregnant, or are you breast-feeding? The amount of insulin you need usually falls during the first three months of pregnancy and increases for the remaining six months. If you are breast-feeding, you may need to alter your insulin intake or diet. Ask your doctor for advice.

Driving and using machines
Your ability to concentrate and react may be reduced if you have hypoglycaemia. Please keep this possible problem in mind in all situations where you might put yourself and others at risk (e.g. driving

a car or operating machinery). You should contact your doctor about the advisability of driving if you have:

- frequent episodes of hypoglycaemia
- reduced or absent warning signs of hypoglycaemia

Humalog Mix25 contains sodium
This medicine contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially 'sodium-free'.

3. How to use Humalog Mix25

The 3 ml cartridge is only for use in Lilly 3 ml pens. It is not for use in 1.5 ml pens.

Always use Humalog Mix25 exactly as your doctor has told you. You should check with your doctor if you are not sure. To prevent the possible transmission of disease, each cartridge must be used by you only, even if the needle on the delivery device is changed.

Dose

- You should normally inject Humalog Mix25 within 15 minutes of a meal. If you need to, you can inject soon after a meal. But your doctor will have told you exactly how much to use, when to use it, and how often. These instructions are only for you. Follow them exactly and visit your diabetes clinic regularly.
- If you change the type of insulin you use (for example from a human or animal insulin to a Humalog product), you may have to take more or less than before. This might just be for the first injection or it may be a gradual change over several weeks or months.
- Inject Humalog Mix25 under the skin. You should not administer it using a different administration route. Under no circumstances should Humalog Mix25 be given intravenously.

Preparing Humalog Mix25

- Cartridges containing Humalog Mix25 should be rotated in the palms of the hands ten times and inverted 180° ten times immediately before use to resuspend insulin until it appears uniformly cloudy or milky. If not, repeat the above procedure until contents are mixed. Cartridges contain a small glass bead to assist mixing. Do not shake vigorously as this may cause frothing which may interfere with the correct measurement of the dose. The cartridges should be examined frequently and should not be used if clumps of material are present or if solid white particles stick to the bottom or wall of the cartridge, giving it a frosted appearance. Check each time you inject yourself.

Getting the pen ready to use

- First wash your hands. Disinfect the rubber membrane of the cartridge.
- **You must only use Humalog Mix25 cartridges in Lilly insulin pens. Please make sure that Humalog or Lilly cartridges are mentioned in the leaflet accompanying your pen. The 3 ml cartridge only fits the 3 ml pen.**
- Follow the instructions that come with the pen. Put the cartridge into the pen.
- You will set the dose to 1 or 2 units. Then hold the pen with the needle pointing up and tap the side of the pen so that any bubbles float to the top. With the pen still pointing up, press the injection mechanism. Do this until a drop of Humalog Mix25 comes out of the needle. There may still be some small air bubbles left in the pen. These are harmless, but if the air bubble is too big, it may make the dose of your injection less accurate.

Injecting Humalog Mix25

- Before you make an injection, clean your skin as you have been instructed. Inject under the skin, as you were taught. Do not inject directly into a vein. After your injection, leave the needle in the skin for five seconds to make sure you have taken the whole dose. Do not rub the area you have just injected. Make sure you inject at least half an inch (1 cm) from the last injection and that you 'rotate' the places you inject, as you have been taught.

After injecting

- As soon as you have done the injection, take the needle off the pen using the outer needle cap. This will keep the Humalog Mix25 sterile and prevent leaking. It will also stop air going back into the pen and the needle clogging up. **Do not share your needles.** Do not share your pen. Replace the cap on your pen. Leave the cartridge in the pen.

Further injections

- Before every injection, dial 1 or 2 units and press the injection mechanism with the pen pointing up until a drop of Humalog Mix25 comes out of the needle. You can see how much Humalog is left by looking at the gauge on the side of the cartridge. The distance between each mark on the gauge is about 20 units. If there is not enough for your dose, change the cartridge.

Do not mix any other insulin in a Humalog Mix25 cartridge. Once the cartridge is empty, do not use it again.

If you use more Humalog Mix25 than you should

If you use more Humalog Mix25 than you need or are unsure how much you have injected, a low blood sugar may occur. Check your blood sugar.

If your blood sugar is low **(mild hypoglycaemia)**, eat glucose tablets, sugar or drink a sugary drink. Then eat fruit, biscuits, or a sandwich, as your doctor has advised you and have some rest. This will often get you over mild hypoglycaemia or a minor insulin overdose. If you get worse and your breathing is shallow and your skin gets pale, tell your doctor at once. A glucagon injection can treat quite severe hypoglycaemia. Eat glucose or sugar after the glucagon injection. If you do not respond to glucagon, you will have to go to hospital. Ask your doctor to tell you about glucagon.

If you forget to use Humalog Mix25

If you take less Humalog Mix25 than you need or are unsure how much you have injected, a high blood sugar may occur. Check your blood sugar

If hypoglycaemia (low blood sugar) or hyperglycaemia (high blood sugar) is not treated they can be very serious and cause headaches, nausea, vomiting, dehydration, unconsciousness, coma or even death (see A and B in section 4 “Possible Side Effects”).

Three simple steps to avoid hypoglycaemia or hyperglycaemia are:

- Always keep spare syringes and a spare vial of Humalog Mix25, or a spare pen and cartridges, in case you lose your pen or cartridges or they get damaged.
- Always carry something to show you are diabetic.
- Always carry sugar with you.

If you stop using Humalog Mix25.

If you take less Humalog Mix25 than you need, a high blood sugar may occur. Do not change your insulin unless your doctor tells you to.

If you have any further questions on the use of this product, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Systemic allergy is rare (≥ 1/10,000 to <1/1,000). The symptoms are as follows:

- rash over the whole body
- difficulty in breathing
- wheezing
- blood pressure dropping
- heart beating fast
- sweating

If you think you are having this sort of insulin allergy with Humalog Mix25, tell your doctor at once.

Local allergy is common (≥ 1/100 to <1/10). Some people get redness, swelling or itching around the area of the insulin injection. This usually clears up in anything from a few days to a few weeks. If this happens to you, tell your doctor.

Lipodystrophy is uncommon (≥ 1/1,000 to <1/100). If you inject insulin too often at the same place, the fatty tissue may either shrink (lipoatrophy) or thicken (lipohypertrophy). Lumps under the skin may also be caused by build-up of a protein called amyloid (cutaneous amyloidosis). The insulin may not work very well if you inject into a lumpy area. Change the injection site with each injection to help prevent these skin changes.

Oedema (e.g. swelling in arms, ankles; fluid retention) has been reported, particularly at the start of insulin therapy or during a change in therapy to improve control of your blood glucose.

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

Common problems of diabetes

A. Hypoglycaemia
Hypoglycaemia (low blood sugar) means there is not enough sugar in the blood. This can be caused if:
- you take too much Humalog Mix25 or other insulin;
- you miss or delay meals or change your diet;
- you exercise or work too hard just before or after a meal;
- you have an infection or illness (especially diarrhoea or vomiting);
- there is a change in your need for insulin; or
- you have trouble with your kidneys or liver which gets worse.

Alcohol and some medicines can affect your blood sugar levels.

The first symptoms of low blood sugar usually come on quickly and include the following:
- tiredness
- nervousness or shakiness
- headache
- rapid heartbeat
- feeling sick
- cold sweat

While you are not confident about recognising your warning symptoms, avoid situations, e.g. driving a car, in which you or others would be put at risk by hypoglycaemia.

B. Hyperglycaemia and diabetic ketoacidosis
Hyperglycaemia (too much sugar in the blood) means that your body does not have enough insulin. Hyperglycaemia can be brought about by:
- not taking your Humalog or other insulin;
- taking less insulin than your doctor tells you to;
- eating a lot more than your diet allows; or
- fever, infection or emotional stress.

Hyperglycaemia can lead to diabetic ketoacidosis. The first symptoms come on slowly over many hours or days. The symptoms include the following:
- feeling sleepy
- flushed face
- thirst
- no appetite
- fruity smell on the breath
- feeling or being sick

Severe symptoms are heavy breathing and a rapid pulse. **Get medical help immediately.**

C. Illness
If you are ill, especially if you feel sick or are sick, the amount of insulin you need may change. **Even when you are not eating normally, you still need insulin.** Test your urine or blood, follow your 'sick rules', and tell your doctor.

5. How to store Humalog Mix25

Before the first use store your Humalog Mix25 in a refrigerator (2°C – 8°C). Do not freeze.

Keep your cartridge in use at room temperature (below 30°C) and discard after 28 days. Do not put it near heat or in the sun. Do not keep your pen or the cartridges you are using in the fridge. The pen with the inserted cartridge should not be stored with the needle attached.

Keep out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the label and the carton. The expiry date refers to the last day of that month.

Do not use this medicine if you notice clumps of material are present or if solid white particles stick to the bottom or wall of the cartridge, giving it a frosted appearance. Check each time you inject yourself.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. Contents of the pack and other information

What Humalog Mix25 100 units/ml suspension for injection in cartridge contains
- The active substance is insulin lispro. Insulin lispro is made in the laboratory by a 'recombinant DNA technology' process. It is a changed form of human insulin and so is different from other human and animal insulins. Insulin lispro is closely related to human insulin which is a natural hormone made by the pancreas.
- The other ingredients are protamine sulphate, m-cresol, phenol, glycerol, dibasic sodium phosphate $7H_2O$, zinc oxide and water for injection. Sodium hydroxide or hydrochloric acid may have been used to adjust the acidity.

What Humalog Mix25 100 units/ml suspension for injection in cartridge looks like and contents of the pack
Humalog Mix25 100 units/ml suspension for injection is a white, sterile suspension and contains 100 units of insulin lispro in each millilitre (100 units/ml) suspension for injection. 25% of the insulin lispro in Humalog Mix25 is dissolved in water. 75% of the insulin lispro in Humalog Mix25 is available in a suspension together with protamine sulphate. Each cartridge contains 300 units (3 millilitres). The cartridges come in packs of 5 or 10 cartridges. Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer
Humalog Mix25 100 units/ml suspension for injection in cartridge is made by:
- Lilly France S.A.S., Rue du Colonel Lilly, 67640 Fegersheim, France,
- Eli Lilly Italia S.p.A., Via Gramsci 731-733, 50019 Sesto Fiorentino, (FI) Italy.

The product licence is held by: Eli Lilly Nederland B.V., Orteliuslaan 1000, 3528 BD Utrecht, The Netherlands.

For any information about this medicinal product, please contact the local representative of the Marketing Authorisation Holder:

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This leaflet was last revised in {MM/YYYY}.

Detailed information on this medicine is available on the European Medicines Agency web site: https://www.ema.europa.eu.

Package leaflet: Information for the user

Humalog Mix50 100 units/ml suspension for injection in cartridge
insulin lispro

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Humalog Mix50 is and what it is used for
2. What you need to know before you use Humalog Mix50
3. How to use Humalog Mix50
4. Possible side effects
5. How to store Humalog Mix50
6. Contents of the pack and other information

1. What Humalog Mix50 is and what it is used for

Humalog Mix50 is used to treat diabetes. Humalog Mix50 is a premixed suspension. Its active substance is insulin lispro. 50% of the insulin lispro in Humalog Mix50 is dissolved in water and it works more quickly than normal human insulin because the insulin molecule has been changed slightly. 50% of the insulin lispro in Humalog Mix50 is available in a suspension together with protamine sulphate, so that its action is prolonged.

You get diabetes if your pancreas does not make enough insulin to control the level of glucose in your blood. Humalog Mix50 is a substitute for your own insulin and is used to control glucose in the long term. Humalog Mix50 works very quickly and longer than soluble insulin. You should normally use Humalog Mix50 within 15 minutes of a meal.

Your doctor may tell you to use Humalog Mix50 as well as a longer-acting insulin. Each kind of insulin comes with another patient information leaflet to tell you about it. Do not change your insulin unless your doctor tells you to. Be very careful if you do change insulin.

2. What you need to know before you use Humalog Mix50

Do NOT use Humalog Mix50
- if you think **hypoglycaemia** (low blood sugar) is starting. Further in this leaflet it tells you how to deal with mild hypoglycaemia (see Section 3: If you take more Humalog Mix50 than you need).
- if you are **allergic** to insulin lispro or any of the other ingredients of this medicine (listed in section 6).

Warnings and precautions
- Always check the pack and the cartridge label for the name and type of the insulin when you get it from your pharmacy. Make sure you get the Humalog Mix50 that your doctor has told you to use.
- If your blood sugar levels are well controlled by your current insulin therapy, you may not feel the warning symptoms when your blood sugar is falling too low. Warning signs are listed later in this leaflet. You must think carefully about when to have your meals, how often to exercise and how

much to do. You must also keep a close watch on your blood sugar levels by testing your blood glucose often.
- A few people who have had hypoglycaemia after switching from animal insulin to human insulin have reported that the early warning symptoms were less obvious or different. If you often have hypoglycaemia or have difficulty recognising them, please discuss this with your doctor.
- If you answer YES to any of the following questions, tell your doctor, pharmacist or diabetes nurse
  - Have you recently become ill?
  - Do you have trouble with your kidneys or liver?
  - Are you exercising more than usual?
- The amount of insulin you need may also change if you drink alcohol.
- You should also tell your doctor, pharmacist or diabetes nurse if you are planning to go abroad. The time difference between countries may mean that you have to have your injections and meals at different times from when you are at home.
- Some patients with long-standing type 2 diabetes mellitus and heart disease or previous stroke who were treated with pioglitazone and insulin experienced the development of heart failure. Inform your doctor as soon as possible, if you experience signs of heart failure such as unusual shortness of breath or rapid increase in weight or localised swelling (oedema).

Skin changes at the injection site
The injection site should be rotated to prevent skin changes such as lumps under the skin. The insulin may not work very well if you inject into a lumpy area (See How to use Humalog Mix50). Contact your doctor if you are currently injecting into a lumpy area before you start injecting a different area. Your doctor may tell you to check your blood sugar more closely, and to adjust your insulin or your other antidiabetic medications dose.

Other medicines and Humalog Mix50
Your insulin needs may change if you are taking
- the contraceptive pill,
- steroids,
- thyroid hormone replacement therapy,
- oral hypoglycaemics,
- acetyl salicylic acid,
- sulpha antibiotics,
- octreotide,
- "beta$_2$ stimulants" (for example ritodrine, salbutamol or terbutaline),
- beta-blockers, or
- some antidepressants (monoamine oxidase inhibitors or selective serotonin reuptake inhibitors),
- danazol,
- some angiotensin converting enzyme (ACE) inhibitors (for example captopril, enalapril), and
- angiotensin II receptor blockers.

Please tell your doctor, if you are taking, have recently taken or might take any other medicines, including medicines obtained without a prescription (see section "Warnings and precautions").

Pregnancy and breast-feeding
Are you pregnant or thinking about becoming pregnant, or are you breast-feeding? The amount of insulin you need usually falls during the first three months of pregnancy and increases for the remaining six months. If you are breast-feeding, you may need to alter your insulin intake or diet. Ask your doctor for advice.

Driving and using machines
Your ability to concentrate and react may be reduced if you have hypoglycaemia. Please keep this possible problem in mind in all situations where you might put yourself and others at risk (e.g. driving

a car or operating machinery). You should contact your doctor about the advisability of driving if you have:

- frequent episodes of hypoglycaemia
- reduced or absent warning signs of hypoglycaemia

Humalog Mix50 contains sodium
This medicine contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially 'sodium-free'.

3. How to use Humalog Mix50

The 3 ml cartridge is only for use in Lilly 3 ml pens. It is not for use in 1.5 ml pens.

Always use Humalog Mix50 exactly as your doctor has told you. You should check with your doctor if you are not sure. To prevent the possible transmission of disease, each cartridge must be used by you only, even if the needle on the delivery device is changed.

Dose

- You should normally inject Humalog Mix50 within 15 minutes of a meal. If you need to, you can inject soon after a meal. But your doctor will have told you exactly how much to use, when to use it, and how often. These instructions are only for you. Follow them exactly and visit your diabetes clinic regularly.
- If you change the type of insulin you use (for example from a human or animal insulin to a Humalog product), you may have to take more or less than before. This might just be for the first injection or it may be a gradual change over several weeks or months.
- Inject Humalog Mix50 under the skin. You should not administer it using a different administration route. Under no circumstances should Humalog Mix50 be given intravenously.

Preparing Humalog Mix50

- Cartridges containing Humalog Mix50 should be rotated in the palms of the hands ten times and inverted 180° ten times immediately before use to resuspend insulin until it appears uniformly cloudy or milky. If not, repeat the above procedure until contents are mixed. Cartridges contain a small glass bead to assist mixing. Do not shake vigorously as this may cause frothing which may interfere with the correct measurement of the dose. The cartridges should be examined frequently and should not be used if clumps of material are present or if solid white particles stick to the bottom or wall of the cartridge, giving it a frosted appearance. Check each time you inject yourself.

Getting the pen ready to use

- First wash your hands. Disinfect the rubber membrane of the cartridge.
- **You must only use Humalog Mix50 cartridges in Lilly insulin pens. Please make sure that Humalog or Lilly cartridges are mentioned in the leaflet accompanying your pen. The 3 ml cartridge only fits the 3 ml pen.**
- Follow the instructions that come with the pen. Put the cartridge into the pen.
- You will set the dose to 1 or 2 units. Then hold the pen with the needle pointing up and tap the side of the pen so that any bubbles float to the top. With the pen still pointing up, press the injection mechanism. Do this until a drop of Humalog Mix50 comes out of the needle. There may still be some small air bubbles left in the pen. These are harmless, but if the air bubble is too big, it may make the dose of your injection less accurate.

Injecting Humalog Mix50

- Before you make an injection, clean your skin as you have been instructed. Inject under the skin, as you were taught. Do not inject directly into a vein. After your injection, leave the needle in the skin for five seconds to make sure you have taken the whole dose. Do not rub the area you have just injected. Make sure you inject at least half an inch (1 cm) from the last injection and that you 'rotate' the places you inject, as you have been taught.

After injecting

- As soon as you have done the injection, take the needle off the pen using the outer needle cap. This will keep the Humalog Mix50 sterile and prevent leaking. It will also stop air going back into the pen and the needle clogging up. **Do not share your needles.** Do not share your pen. Replace the cap on your pen. Leave the cartridge in the pen.

Further injections

- Before every injection, dial 1 or 2 units and press the injection mechanism with the pen pointing up until a drop of Humalog Mix50 comes out of the needle. You can see how much Humalog is left by looking at the gauge on the side of the cartridge. The distance between each mark on the gauge is about 20 units. If there is not enough for your dose, change the cartridge.

Do not mix any other insulin in a Humalog Mix50 cartridge. Once the cartridge is empty, do not use it again.

If you use more Humalog Mix50 than you should

If you use more Humalog Mix50 than you need or are unsure how much you have injected, a low blood sugar may occur. Check your blood sugar.

If your blood sugar is low **(mild hypoglycaemia)**, eat glucose tablets, sugar or drink a sugary drink. Then eat fruit, biscuits, or a sandwich, as your doctor has advised you and have some rest. This will often get you over mild hypoglycaemia or a minor insulin overdose. If you get worse and your breathing is shallow and your skin gets pale, tell your doctor at once. A glucagon injection can treat quite severe hypoglycaemia. Eat glucose or sugar after the glucagon injection. If you do not respond to glucagon, you will have to go to hospital. Ask your doctor to tell you about glucagon.

If you forget to use Humalog Mix50

If you take less Humalog Mix50 than you need or are unsure how much you have injected, a high blood sugar may occur. Check your blood sugar

If hypoglycaemia (low blood sugar) or hyperglycaemia (high blood sugar) is not treated they can be very serious and cause headaches, nausea, vomiting, dehydration, unconsciousness, coma or even death (see A and B in section 4 “Possible Side Effects”).

Three simple steps to avoid hypoglycaemia or hyperglycaemia are:

- Always keep a spare pen and cartridges, in case you lose your pen or cartridges or they get damaged.
- Always carry something to show you are diabetic.
- Always carry sugar with you.

If you stop using Humalog Mix50.

If you take less Humalog Mix50 than you need, a high blood sugar may occur. Do not change your insulin unless your doctor tells you to.

If you have any further questions on the use of this product, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Systemic allergy is rare (≥ 1/10,000 to <1/1,000). The symptoms are as follows:

- rash over the whole body
- difficulty in breathing
- wheezing
- blood pressure dropping
- heart beating fast
- sweating

If you think you are having this sort of insulin allergy with Humalog Mix50, tell your doctor at once.

Local allergy is common (≥ 1/100 to <1/10). Some people get redness, swelling or itching around the area of the insulin injection. This usually clears up in anything from a few days to a few weeks. If this happens to you, tell your doctor.

Lipodystrophy is uncommon (≥ 1/1,000 to <1/100). If you inject insulin too often at the same place, the fatty tissue may either shrink (lipoatrophy) or thicken (lipohypertrophy). Lumps under the skin may also be caused by build-up of a protein called amyloid (cutaneous amyloidosis). The insulin may not work very well if you inject into a lumpy area. Change the injection site with each injection to help prevent these skin changes.

Oedema (e.g. swelling in arms, ankles; fluid retention) has been reported, particularly at the start of insulin therapy or during a change in therapy to improve control of your blood glucose.

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

Common problems of diabetes

A. Hypoglycaemia
Hypoglycaemia (low blood sugar) means there is not enough sugar in the blood. This can be caused if:
- you take too much Humalog Mix50 or other insulin;
- you miss or delay meals or change your diet;
- you exercise or work too hard just before or after a meal;
- you have an infection or illness (especially diarrhoea or vomiting);
- there is a change in your need for insulin; or
- you have trouble with your kidneys or liver which gets worse.

Alcohol and some medicines can affect your blood sugar levels.

The first symptoms of low blood sugar usually come on quickly and include the following:
- tiredness
- nervousness or shakiness
- headache
- rapid heartbeat
- feeling sick
- cold sweat

While you are not confident about recognising your warning symptoms, avoid situations, e.g. driving a car, in which you or others would be put at risk by hypoglycaemia.

B. Hyperglycaemia and diabetic ketoacidosis
Hyperglycaemia (too much sugar in the blood) means that your body does not have enough insulin. Hyperglycaemia can be brought about by:
- not taking your Humalog or other insulin;
- taking less insulin than your doctor tells you to;
- eating a lot more than your diet allows; or
- fever, infection or emotional stress.

Hyperglycaemia can lead to diabetic ketoacidosis. The first symptoms come on slowly over many hours or days. The symptoms include the following:
- feeling sleepy
- flushed face
- thirst
- no appetite
- fruity smell on the breath
- feeling or being sick

Severe symptoms are heavy breathing and a rapid pulse. **Get medical help immediately.**

C. Illness
If you are ill, especially if you feel sick or are sick, the amount of insulin you need may change. **Even when you are not eating normally, you still need insulin.** Test your urine or blood, follow your 'sick rules', and tell your doctor.

5. How to store Humalog Mix50

Before the first use store your Humalog Mix50 in a refrigerator (2°C – 8°C). Do not freeze.

Keep your cartridge in use at room temperature (below 30°C) and discard after 28 days. Do not put it near heat or in the sun. Do not keep your pen or the cartridges you are using in the fridge. The pen with the inserted cartridge should not be stored with the needle attached.

Keep out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the label and the carton. The expiry date refers to the last day of that month.

Do not use this medicine if you notice clumps of material are present or if solid white particles stick to the bottom or wall of the cartridge, giving it a frosted appearance. Check each time you inject yourself.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. Contents of the pack and other information

What Humalog Mix50 100 units/ml suspension for injection in cartridge contains
- The active substance is insulin lispro. Insulin lispro is made in the laboratory by a 'recombinant DNA technology' process. It is a changed form of human insulin and so is different from other human and animal insulins. Insulin lispro is closely related to human insulin which is a natural hormone made by the pancreas.
- The other ingredients are protamine sulphate, m-cresol, phenol, glycerol, dibasic sodium phosphate $7H_2O$, zinc oxide and water for injection. Sodium hydroxide or hydrochloric acid may have been used to adjust the acidity.

What Humalog Mix50 100 units/ml suspension for injection in cartridge looks like and contents of the pack
Humalog Mix50 100 units/ml suspension for injection is a white, sterile suspension and contains 100 units of insulin lispro in each millilitre (100 units/ml) suspension for injection. 50% of the insulin lispro in Humalog Mix50 is dissolved in water. 50% of the insulin lispro in Humalog Mix50 is available in a suspension together with protamine sulphate. Each cartridge contains 300 units (3 millilitres). The cartridges come in packs of 5 or 10 cartridges. Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer
Humalog Mix50 100 units/ml suspension for injection in cartridge is made by:
- Lilly France S.A.S., Rue du Colonel Lilly, 67640 Fegersheim, France,
- Eli Lilly Italia S.p.A., Via Gramsci 731-733, 50019 Sesto Fiorentino, (FI) Italy.

The product licence is held by: Eli Lilly Nederland B.V., Orteliuslaan 1000, 3528 BD Utrecht, The Netherlands.

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This leaflet was last revised in {MM/YYYY}.

Detailed information on this medicine is available on the European Medicines Agency web site: https://www.ema.europa.eu.

Package leaflet: Information for the user

Humalog 100 units/ml KwikPen solution for injection in a pre-filled pen
insulin lispro
Each KwikPen delivers 1 – 60 units in steps of 1 units.

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Humalog KwikPen is and what it is used for
2. What you need to know before you use Humalog KwikPen
3. How to use Humalog KwikPen
4. Possible side effects
5. How to store Humalog KwikPen
6. Contents of the pack and other information

1. What Humalog KwikPen is and what it is used for

Humalog KwikPen is used to treat diabetes. It works more quickly than normal human insulin because the insulin molecule has been changed slightly.

You get diabetes if your pancreas does not make enough insulin to control the level of glucose in your blood. Humalog is a substitute for your own insulin and is used to control glucose in the long term. It works very quickly and lasts a shorter time than soluble insulin (2 to 5 hours). You should normally use Humalog within 15 minutes of a meal.

Your doctor may tell you to use Humalog KwikPen as well as a longer-acting insulin. Each kind of insulin comes with another patient information leaflet to tell you about it. Do not change your insulin unless your doctor tells you to. Be very careful if you do change insulin.

Humalog is suitable for use in adults and children.

The KwikPen is a disposable pre-filled pen containing 3 ml (300 units, 100 units/ml) of insulin lispro. One KwikPen contains multiple doses of insulin. The KwikPen dials 1 unit at a time. **The number of units are displayed in the dose window, always check this before your injection.** You can give from 1 to 60 units in a single injection. **If your dose is more than 60 units, you will need to give yourself more than one injection.**

2. What you need to know before you use Humalog KwikPen

Do NOT use Humalog KwikPen
- if you think **hypoglycaemia** (low blood sugar) is starting. Further in this leaflet it tells you how to deal with mild hypoglycaemia (see Section 3: If you use more Humalog than you should).
- if you are **allergic** to insulin lispro or any of the other ingredients of this medicine (listed in section 6).

Warnings and precautions

- Always check the pack and the label of the pre-filled pen for the name and type of the insulin when you get it from your pharmacy. Make sure you get the Humalog KwikPen that your doctor has told you to use.
- If your blood sugar levels are well controlled by your current insulin therapy, you may not feel the warning symptoms when your blood sugar is falling too low. Warning signs are listed later in this leaflet. You must think carefully about when to have your meals, how often to exercise and how much to do. You must also keep a close watch on your blood sugar levels by testing your blood glucose often.
- A few people who have had hypoglycaemia after switching from animal insulin to human insulin have reported that the early warning symptoms were less obvious or different. If you often have hypoglycaemia or have difficulty recognising it, please discuss this with your doctor.
- If you answer YES to any of the following questions, tell your doctor, pharmacist or diabetes nurse
  - Have you recently become ill?
  - Do you have trouble with your kidneys or liver?
  - Are you exercising more than usual?
- The amount of insulin you need may also change if you drink alcohol.
- You should also tell your doctor, pharmacist or diabetes nurse if you are planning to go abroad. The time difference between countries may mean that you have to have your injections and meals at different times from when you are at home.
- Some patients with long-standing type 2 diabetes mellitus and heart disease or previous stroke who were treated with pioglitazone and insulin experienced the development of heart failure. Inform your doctor as soon as possible, if you experience signs of heart failure such as unusual shortness of breath or rapid increase in weight or localised swelling (oedema).
- This Pen is not recommended for use by the blind or visually impaired without the help of someone trained to use the Pen.

Skin changes at the injection site

The injection site should be rotated to prevent skin changes such as lumps under the skin. The insulin may not work very well if you inject into a lumpy area (See How to use Humalog KwikPen). Contact your doctor if you are currently injecting into a lumpy area before you start injecting a different area. Your doctor may tell you to check your blood sugar more closely, and to adjust your insulin or your other antidiabetic medications dose.

Other medicines and Humalog KwikPen

Your insulin needs may change if you are taking

- the contraceptive pill,
- steroids,
- thyroid hormone replacement therapy,
- oral hypoglycaemics,
- acetyl salicylic acid,
- sulpha antibiotics,
- octreotide,
- "beta$_2$ stimulants" (for example ritodrine, salbutamol or terbutaline),
- beta-blockers, or
- some antidepressants (monoamine oxidase inhibitors or selective serotonin reuptake inhibitors),
- danazol,
- some angiotensin converting enzyme (ACE) inhibitors (for example captopril, enalapril), and
- angiotensin II receptor blockers.

Please tell your doctor, if you are taking, have recently taken or might take any other medicines, including medicines obtained without a prescription (see section "Warnings and precautions").

Pregnancy and breast-feeding
Are you pregnant or thinking about becoming pregnant, or are you breast-feeding? The amount of insulin you need usually falls during the first three months of pregnancy and increases for the remaining six months. If you are breast-feeding, you may need to alter your insulin intake or diet. Ask your doctor for advice.

Driving and using machines
Your ability to concentrate and react may be reduced if you have hypoglycaemia. Please keep this possible problem in mind in all situations where you might put yourself and others at risk (e.g. driving a car or operating machinery). You should contact your doctor about the advisability of driving if you have:
- frequent episodes of hypoglycaemia
- reduced or absent warning signs of hypoglycaemia

Humalog KwikPen contains sodium
This medicine contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially 'sodium-free'.

3. How to use Humalog KwikPen

Always use Humalog KwikPen exactly as your doctor has told you. You should check with your doctor if you are not sure. To prevent the possible transmission of disease, each pen must be used by you only, even if the needle is changed.

Dose
- You should normally inject Humalog within 15 minutes of a meal. If you need to, you can inject soon after a meal. But your doctor will have told you exactly how much to use, when to use it, and how often. These instructions are only for you. Follow them exactly and visit your diabetes clinic regularly.
- If you change the type of insulin you use (for example from a human or animal insulin to a Humalog product), you may have to take more or less than before. This might just be for the first injection or it may be a gradual change over several weeks or months.
- Humalog KwikPen is only suitable for injecting just under the skin. Speak to your doctor if you need to inject your insulin by another method.

Preparing Humalog KwikPen
- Humalog is already dissolved in water, so you do not need to mix it. But you must use it **only** if it looks like water. It must be clear, have no colour and no solid pieces in it. Check each time you inject yourself.

Getting the KwikPen ready to use (Please see user manual)
- First wash your hands.
- Read the instructions on how to use your pre-filled insulin pen. Please follow the instructions carefully. Here are some reminders.
- Use a clean needle. (Needles are not included).
- Prime your KwikPen before each use. This checks that insulin comes out and clears the air bubbles from your KwikPen. There may still be some small air bubbles left in the pen - these are harmless. But if the air bubbles are too large it may affect the insulin dose.

Injecting Humalog
- Before you make an injection, clean your skin as you have been instructed. Inject under the skin, as you were taught. Do not inject directly into a vein. After your injection, leave the needle in the skin for five seconds to make sure you have taken the whole dose. Do not rub the area you have just injected. Make sure you inject at least half an inch (1 cm) from the last injection and that you 'rotate' the places you inject, as you have been taught. It doesn't matter which

injection site you use, either upper arm, thigh, buttock or abdomen, your Humalog injection will still work quicker than soluble human insulin.

- You must not administer Humalog by the intravenous route. Inject Humalog as your physician or nurse has taught you. Only your physician can administer Humalog by the intravenous route. He will only do this under special circumstances such as surgery or if you are ill and your glucose levels are too high.

After injecting

- As soon as you have done the injection, unscrew the needle from the KwikPen using the outer needle cap. This will keep the insulin sterile and stop it leaking. It also stops air entering the pen and your needle clogging. **Do not share your needles**. Do not share your pen. Replace the cap on your pen.

Further injections

- Every time you use a KwikPen you must use a new needle. Before every injection, clear any air bubbles. You can see how much insulin is left by holding the KwikPen with the needle pointing up. The scale on the cartridge shows about how many units you have left.
- Do not mix any other insulin in your disposable pen. Once the KwikPen is empty, do not use it again. Please get rid of it carefully - your pharmacist or diabetes nurse will tell you how to do this.

Using Humalog in an infusion pump

- KwikPen is only suitable for injecting just under the skin. Do not use the pen to administer Humalog by a different way. Other forms of Humalog 100 units/ml are available if this is necessary. Speak to your doctor if this applies to you.

If you use more Humalog than you should

If you use more Humalog than you need or are unsure how much you have injected, a low blood sugar may occur. Check your blood sugar.

If your blood sugar is low **(mild hypoglycaemia)**, eat glucose tablets, sugar or drink a sugary drink. Then eat fruit, biscuits, or a sandwich, as your doctor has advised you and have some rest. This will often get you over mild hypoglycaemia or a minor insulin overdose. If you get worse and your breathing is shallow and your skin gets pale, tell your doctor at once. A glucagon injection can treat quite severe hypoglycaemia. Eat glucose or sugar after the glucagon injection. If you do not respond to glucagon, you will have to go to hospital. Ask your doctor to tell you about glucagon.

If you forget to use Humalog

If you take less Humalog than you need or are unsure how much you have injected, a high blood sugar may occur. Check your blood sugar

If hypoglycaemia (low blood sugar) or hyperglycaemia (high blood sugar) is not treated they can be very serious and cause headaches, nausea, vomiting, dehydration, unconsciousness, coma or even death (see A and B in section 4 “Possible Side Effects”).

Three simple steps to avoid hypoglycaemia or hyperglycaemia are:

- Always keep spare syringes and a spare vial of Humalog, or a spare pen and cartridges, in case you lose your KwikPen or it gets damaged.
- Always carry something to show you are diabetic.
- Always carry sugar with you.

If you stop using Humalog.

If you take less Humalog than you need, a high blood sugar may occur. Do not change your insulin unless your doctor tells you to.

If you have any further questions on the use of this product, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Systemic allergy is rare (≥ 1/10,000 to <1/1,000). The symptoms are as follows:

- rash over the whole body
- difficulty in breathing
- wheezing
- blood pressure dropping
- heart beating fast
- sweating

If you think you are having this sort of insulin allergy with Humalog, tell your doctor at once.

Local allergy is common (≥ 1/100 to <1/10). Some people get redness, swelling or itching around the area of the insulin injection. This usually clears up in anything from a few days to a few weeks. If this happens to you, tell your doctor.

Lipodystrophy is uncommon (≥ 1/1,000 to <1/100). If you inject insulin too often at the same place, the fatty tissue may either shrink (lipoatrophy) or thicken (lipohypertrophy). Lumps under the skin may also be caused by build-up of a protein called amyloid (cutaneous amyloidosis). The insulin may not work very well if you inject into a lumpy area. Change the injection site with each injection to help prevent these skin changes.

Oedema (e.g. swelling in arms, ankles; fluid retention) has been reported, particularly at the start of insulin therapy or during a change in therapy to improve control of your blood glucose.

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

Common problems of diabetes

A. Hypoglycaemia

Hypoglycaemia (low blood sugar) means there is not enough sugar in the blood. This can be caused if:

- you take too much Humalog or other insulin;
- you miss or delay meals or change your diet;
- you exercise or work too hard just before or after a meal;
- you have an infection or illness (especially diarrhoea or vomiting);
- there is a change in your need for insulin; or
- you have trouble with your kidneys or liver which gets worse.

Alcohol and some medicines can affect your blood sugar levels.

The first symptoms of low blood sugar usually come on quickly and include the following:

- tiredness
- nervousness or shakiness
- headache
- rapid heartbeat
- feeling sick
- cold sweat

While you are not confident about recognising your warning symptoms, avoid situations, e.g. driving a car, in which you or others would be put at risk by hypoglycaemia.

B. Hyperglycaemia and diabetic ketoacidosis

Hyperglycaemia (too much sugar in the blood) means that your body does not have enough insulin. Hyperglycaemia can be brought about by:

- not taking your Humalog or other insulin;
- taking less insulin than your doctor tells you to;

- eating a lot more than your diet allows; or
- fever, infection or emotional stress.

Hyperglycaemia can lead to diabetic ketoacidosis. The first symptoms come on slowly over many hours or days. The symptoms include the following:

- feeling sleepy
- flushed face
- thirst
- no appetite
- fruity smell on the breath
- feeling or being sick

Severe symptoms are heavy breathing and a rapid pulse. **Get medical help immediately.**

C. Illness

If you are ill, especially if you feel sick or are sick, the amount of insulin you need may change. **Even when you are not eating normally, you still need insulin.** Test your urine or blood, follow your 'sick rules', and tell your doctor.

5. How to store Humalog KwikPen

Before the first use store your Humalog KwikPen in a refrigerator (2°C – 8°C). Do not freeze.

Keep your Humalog KwikPen in use at room temperature (below 30°C) and discard after 28 days. Do not put it near heat or in the sun. Do not keep the KwikPen that you are using in the fridge. The KwikPen should not be stored with the needle attached.

Keep out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the label and the carton. The expiry date refers to the last day of that month.

Do not use this medicine if you notice the solution is coloured or it has solid pieces in it. You must use it **only** if it looks like water. Check this each time you inject yourself.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. Contents of the pack and other information

What Humalog 100 units/ml KwikPen solution for injection contains

- The active substance is insulin lispro. Insulin lispro is made in the laboratory by a 'recombinant DNA technology' process. It is a changed form of human insulin and so is different from other human and animal insulins. Insulin lispro is closely related to human insulin which is a natural hormone made by the pancreas.
- The other ingredients are m-cresol, glycerol, dibasic sodium phosphate 7 H_2O, zinc oxide and water for injection. Sodium hydroxide or hydrochloric acid may have been used to adjust the acidity.

What Humalog KwikPen looks like and contents of the pack

Humalog 100 units/ml KwikPen solution for injection is a sterile, clear, colourless, aqueous solution and contains 100 units of insulin lispro in each millilitre (100 units/ml) solution for injection. Each Humalog KwikPen contains 300 units (3 millilitres). The Humalog KwikPen comes in a pack of 5 pre-filled pens or a multipack of 2 x 5 pre-filled pens. Not all pack sizes may be marketed. The Humalog 100 units/ml in your pre-filled pen is the same as the Humalog 100 units/ml, which comes in separate Humalog 100 units/ml cartridges. The KwikPen simply has a built in cartridge. When the pre-filled pen is empty you cannot use it again.

Marketing Authorisation Holder and Manufacturer
Humalog 100 units/ml KwikPen solution for injection is made by:

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This leaflet was last revised in {MM/YYYY}.

USER MANUAL

Please see manual text later.

Detailed information on this medicine is available on the European Medicines Agency web site: https://www.ema.europa.eu.

Package leaflet: Information for the user

Humalog Mix25 100 units/ml KwikPen suspension for injection in a pre-filled pen
insulin lispro
Each KwikPen delivers 1 – 60 units in steps of 1 units.

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Humalog Mix25 KwikPen is and what it is used for
2. What you need to know before you use Humalog Mix25 KwikPen
3. How to use Humalog Mix25 KwikPen
4. Possible side effects
5. How to store Humalog Mix25 KwikPen
6. Contents of the pack and other information

1. What Humalog Mix25 KwikPen is and what it is used for

Humalog Mix25 KwikPen is used to treat diabetes. It is a premixed suspension. Its active substance is insulin lispro. 25% of the insulin lispro in Humalog Mix25 KwikPen is dissolved in water and it works more quickly than normal human insulin because the insulin molecule has been changed slightly. 75% of the insulin lispro in Humalog Mix25 KwikPen is available in a suspension together with protamine sulphate, so that its action is prolonged.

You get diabetes if your pancreas does not make enough insulin to control the level of glucose in your blood. Humalog Mix25 is a substitute for your own insulin and is used to control glucose in the long term. Humalog Mix25 works very quickly and longer than soluble insulin. You should normally use Humalog Mix25 within 15 minutes of a meal.

Your doctor may tell you to use Humalog Mix25 KwikPen as well as a longer-acting insulin. Each kind of insulin comes with another patient information leaflet to tell you about it. Do not change your insulin unless your doctor tells you to. Be very careful if you do change insulin.

The KwikPen is a disposable pre-filled pen containing 3 ml (300 units, 100 units/ml) of insulin lispro. One KwikPen contains multiple doses of insulin. The KwikPen dials 1 unit at a time. **The number of units are displayed in the dose window, always check this before your injection.** You can give from 1 to 60 units in a single injection. **If your dose is more than 60 units, you will need to give yourself more than one injection.**

2. What you need to know before you use Humalog Mix25 KwikPen

Do NOT use Humalog Mix25 KwikPen
- if you think **hypoglycaemia** (low blood sugar) is starting. Further in this leaflet it tells you how to deal with mild hypoglycaemia (see Section 3: If you take more Humalog Mix25 than you need).
- if you are **allergic** to insulin lispro or any of the other ingredients of this medicine (listed in section 6).

Warnings and precautions

- Always check the pack and the label of the pre-filled pen for the name and type of the insulin when you get it from your pharmacy. Make sure you get the Humalog Mix25 KwikPen that your doctor has told you to use.
- If your blood sugar levels are well controlled by your current insulin therapy, you may not feel the warning symptoms when your blood sugar is falling too low. Warning signs are listed later in this leaflet. You must think carefully about when to have your meals, how often to exercise and how much to do. You must also keep a close watch on your blood sugar levels by testing your blood glucose often.
- A few people who have had hypoglycaemia after switching from animal insulin to human insulin have reported that the early warning symptoms were less obvious or different. If you often have hypoglycaemia or have difficulty recognising them, please discuss this with your doctor.
- If you answer YES to any of the following questions, tell your doctor, pharmacist or diabetes nurse
  - Have you recently become ill?
  - Do you have trouble with your kidneys or liver?
  - Are you exercising more than usual?
- The amount of insulin you need may also change if you drink alcohol.
- You should also tell your doctor, pharmacist or diabetes nurse if you are planning to go abroad. The time difference between countries may mean that you have to have your injections and meals at different times from when you are at home.
- Some patients with long-standing type 2 diabetes mellitus and heart disease or previous stroke who were treated with pioglitazone and insulin experienced the development of heart failure. Inform your doctor as soon as possible, if you experience signs of heart failure such as unusual shortness of breath or rapid increase in weight or localised swelling (oedema).
- This Pen is not recommended for use by the blind or visually impaired without the help of someone trained to use the Pen.

Skin changes at the injection site

The injection site should be rotated to prevent skin changes such as lumps under the skin. The insulin may not work very well if you inject into a lumpy area (See How to use Humalog Mix25 KwikPen). Contact your doctor if you are currently injecting into a lumpy area before you start injecting a different area. Your doctor may tell you to check your blood sugar more closely, and to adjust your insulin or your other antidiabetic medications dose.

Other medicines and Humalog Mix25 KwikPen

Your insulin needs may change if you are taking

- the contraceptive pill,
- steroids,
- thyroid hormone replacement therapy,
- oral hypoglycaemics,
- acetyl salicylic acid,
- sulpha antibiotics,
- octreotide,
- "beta$_2$ stimulants" (for example ritodrine, salbutamol or terbutaline),
- beta-blockers, or
- some antidepressants (monoamine oxidase inhibitors or selective serotonin reuptake inhibitors),
- danazol,
- some angiotensin converting enzyme (ACE) inhibitors (for example captopril, enalapril), and
- angiotensin II receptor blockers.

Please tell your doctor, if you are taking, have recently taken or might take any other medicines, including medicines obtained without a prescription (see section "Warnings and precautions").

Pregnancy and breast-feeding
Are you pregnant or thinking about becoming pregnant, or are you breast-feeding? The amount of insulin you need usually falls during the first three months of pregnancy and increases for the remaining six months. If you are breast-feeding, you may need to alter your insulin intake or diet. Ask your doctor for advice.

Driving and using machines
Your ability to concentrate and react may be reduced if you have hypoglycaemia. Please keep this possible problem in mind in all situations where you might put yourself and others at risk (e.g. driving a car or operating machinery). You should contact your doctor about the advisability of driving if you have:

- frequent episodes of hypoglycaemia
- reduced or absent warning signs of hypoglycaemia

Humalog Mix25 KwikPen contains sodium
This medicine contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially 'sodium-free'.

3. How to use Humalog Mix25 KwikPen

Always use Humalog Mix25 KwikPen exactly as your doctor has told you. You should check with your doctor if you are not sure. To prevent the possible transmission of disease, each pen must be used by you only, even if the needle is changed.

Dose

- You should normally inject Humalog Mix25 within 15 minutes of a meal. If you need to, you can inject soon after a meal. But your doctor will have told you exactly how much to use, when to use it, and how often. These instructions are only for you. Follow them exactly and visit your diabetes clinic regularly.
- If you change the type of insulin you use (for example from a human or animal insulin to a Humalog product), you may have to take more or less than before. This might just be for the first injection or it may be a gradual change over several weeks or months.
- Humalog Mix25 KwikPen is only suitable for injecting just under the skin. Speak to your doctor if you need to inject your insulin by another method.

Preparing Humalog Mix25 KwikPen

- The KwikPen should be rotated in the palms of the hands ten times and inverted 180° ten times immediately before use to resuspend insulin until it appears uniformly cloudy or milky. If not, repeat the above procedure until contents are mixed. Cartridges contain a small glass bead to assist mixing. Do not shake vigorously as this may cause frothing which may interfere with the correct measurement of the dose. The cartridges should be examined frequently and should not be used if clumps of material are present or if solid white particles stick to the bottom or wall of the cartridge, giving it a frosted appearance. Check each time you inject yourself.

Getting the KwikPen ready to use (Please see user manual)

- First wash your hands.
- Read the instructions on how to use your pre-filled insulin pen. Please follow the instructions carefully. Here are some reminders.
- Use a clean needle. (Needles are not included).
- Prime your KwikPen before each use. This checks that insulin comes out and clears the air bubbles from your KwikPen. There may still be some small air bubbles left in the pen - these are harmless. But if the air bubbles are too large it may affect the insulin dose.

Injecting Humalog Mix25

- Before you make an injection, clean your skin as you have been instructed. Inject under the skin, as you were taught. Do not inject directly into a vein. After your injection, leave the

needle in the skin for five seconds to make sure you have taken the whole dose. Do not rub the area you have just injected. Make sure you inject at least half an inch (1 cm) from where you last injected and that you 'rotate' the places you inject, as you have been taught.

After injecting

- As soon as you have done the injection, unscrew the needle from the KwikPen using the outer needle cap. This will keep the insulin sterile and stop it leaking. It also stops air entering the pen and your needle clogging**. Do not share your needles**. Do not share your pen. Replace the cap on the pen.

Further injections

- Every time you use a KwikPen you must use a new needle. Before every injection, clear any air bubbles. You can see how much insulin is left by holding the KwikPen with the needle pointing up. The scale on the cartridge shows about how many units you have left.
- Do not mix any other insulin in your disposable pen. Once the KwikPen is empty, do not use it again. Please get rid of it carefully - your pharmacist or diabetes nurse will tell you how to do this.

If you use more Humalog Mix25 than you should

If you use more Humalog Mix25 than you need or are unsure how much you have injected, a low blood sugar may occur. Check your blood sugar.

If your blood sugar is low **(mild hypoglycaemia)**, eat glucose tablets, sugar or drink a sugary drink. Then eat fruit, biscuits, or a sandwich, as your doctor has advised you and have some rest. This will often get you over mild hypoglycaemia or a minor insulin overdose. If you get worse and your breathing is shallow and your skin gets pale, tell your doctor at once. A glucagon injection can treat quite severe hypoglycaemia. Eat glucose or sugar after the glucagon injection. If you do not respond to glucagon, you will have to go to hospital. Ask your doctor to tell you about glucagon.

If you forget to use Humalog Mix25

If you take less Humalog Mix25 than you need or are unsure how much you have injected, a high blood sugar may occur. Check your blood sugar

If hypoglycaemia (low blood sugar) or hyperglycaemia (high blood sugar) is not treated they can be very serious and cause headaches, nausea, vomiting, dehydration, unconsciousness, coma or even death (see A and B in section 4 "Possible Side Effects").

Three simple steps to avoid hypoglycaemia or hyperglycaemia are:

- Always keep spare syringes and a spare vial of Humalog Mix25, or a spare pen and cartridges, in case you lose your KwikPen or it gets damaged.
- Always carry something to show you are diabetic.
- Always carry sugar with you.

If you stop using Humalog Mix25.

If you take less Humalog Mix25 than you need, a high blood sugar may occur. Do not change your insulin unless your doctor tells you to.

If you have any further questions on the use of this product, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Systemic allergy is rare (≥ 1/10,000 to <1/1,000). The symptoms are as follows:
- rash over the whole body
- difficulty in breathing
- wheezing
- blood pressure dropping
- heart beating fast
- sweating

If you think you are having this sort of insulin allergy with Humalog Mix25, tell your doctor at once.

Local allergy is common (≥ 1/100 to <1/10). Some people get redness, swelling or itching around the area of the insulin injection. This usually clears up in anything from a few days to a few weeks. If this happens to you, tell your doctor.

Lipodystrophy is uncommon (≥ 1/1,000 to <1/100). If you inject insulin too often at the same place, the fatty tissue may either shrink (lipoatrophy) or thicken (lipohypertrophy). Lumps under the skin may also be caused by build-up of a protein called amyloid (cutaneous amyloidosis). The insulin may not work very well if you inject into a lumpy area. Change the injection site with each injection to help prevent these skin changes.

Oedema (e.g. swelling in arms, ankles; fluid retention) has been reported, particularly at the start of insulin therapy or during a change in therapy to improve control of your blood glucose.

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

Common problems of diabetes

A. Hypoglycaemia
Hypoglycaemia (low blood sugar) means there is not enough sugar in the blood. This can be caused if:
- you take too much Humalog Mix25 or other insulin;
- you miss or delay meals or change your diet;
- you exercise or work too hard just before or after a meal;
- you have an infection or illness (especially diarrhoea or vomiting);
- there is a change in your need for insulin; or
- you have trouble with your kidneys or liver which gets worse.

Alcohol and some medicines can affect your blood sugar levels.

The first symptoms of low blood sugar usually come on quickly and include the following:
- tiredness
- nervousness or shakiness
- headache
- rapid heartbeat
- feeling sick
- cold sweat

While you are not confident about recognising your warning symptoms, avoid situations, e.g. driving a car, in which you or others would be put at risk by hypoglycaemia.

B. Hyperglycaemia and diabetic ketoacidosis
Hyperglycaemia (too much sugar in the blood) means that your body does not have enough insulin. Hyperglycaemia can be brought about by:
- not taking your Humalog or other insulin;
- taking less insulin than your doctor tells you to;
- eating a lot more than your diet allows; or
- fever, infection or emotional stress.

Hyperglycaemia can lead to diabetic ketoacidosis. The first symptoms come on slowly over many hours or days. The symptoms include the following:
- feeling sleepy
- no appetite

- flushed face
- thirst
- fruity smell on the breath
- feeling or being sick

Severe symptoms are heavy breathing and a rapid pulse. **Get medical help immediately.**

C. Illness
If you are ill, especially if you feel sick or are sick, the amount of insulin you need may change. **Even when you are not eating normally, you still need insulin.** Test your urine or blood, follow your 'sick rules', and tell your doctor.

5. How to store Humalog Mix25 KwikPen

Before the first use store your Humalog Mix25 KwikPen in a refrigerator (2°C – 8°C). Do not freeze.

Keep your Humalog Mix25 KwikPen in use at room temperature (below 30°C) and discard after 28 days. Do not put it near heat or in the sun. Do not keep the KwikPen that you are using in the fridge. The KwikPen should not be stored with the needle attached.

Keep out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the label and the carton. The expiry date refers to the last day of that month.

Do not use this medicine if you notice clumps of material are present or if solid white particles stick to the bottom or wall of the cartridge, giving it a frosted appearance. Check each time you inject yourself.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. Contents of the pack and other information

What Humalog Mix25 100 units/ml KwikPen suspension for injection contains
- The active substance is insulin lispro. Insulin lispro is made in the laboratory by a 'recombinant DNA technology' process. It is a changed form of human insulin and so is different from other human and animal insulins. Insulin lispro is closely related to human insulin which is a natural hormone made by the pancreas.
- The other ingredients are protamine sulphate, m-cresol, phenol, glycerol, dibasic sodium phosphate $7H_2O$, zinc oxide and water for injection. Sodium hydroxide or hydrochloric acid may have been used to adjust the acidity.

What Humalog Mix25 100 units/ml KwikPen suspension for injection looks like and contents of the pack
Humalog Mix25 100 units/ KwikPen suspension for injection is a white, sterile suspension and contains 100 units of insulin lispro in each millilitre (100 units/ml) suspension for injection. 25% of the insulin lispro in Humalog Mix25 is dissolved in water. 75% of the insulin lispro in Humalog Mix25 is available in a suspension together with protamine sulphate. Each Humalog Mix25 KwikPen contains 300 units (3 millilitres). The Humalog Mix25 KwikPen comes in a pack of 5 pre-filled pens or a multipack of 2 x 5 pre-filled pens. Not all pack sizes may be marketed. The Humalog Mix25 in your KwikPen is the same as the Humalog Mix25, which comes in separate Humalog Mix25 cartridges. The KwikPen simply has a built in cartridge. When the KwikPen is empty you cannot use it again.

Marketing Authorisation Holder and Manufacturer
Humalog Mix25 100 units/ml KwikPen suspension for injection is made by:
- Lilly France S.A.S., Rue du Colonel Lilly, 67640 Fegersheim, France,

- Eli Lilly Italia S.p.A., Via Gramsci 731-733, 50019 Sesto Fiorentino, (FI) Italy.

The product licence is held by: Eli Lilly Nederland B.V., Orteliuslaan 1000, 3528 BD Utrecht, The Netherlands.

For any information about this medicinal product, please contact the local representative of the Marketing Authorisation Holder:

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This leaflet was last revised in {MM/YYYY}.

USER MANUAL

Please see manual text later.

Detailed information on this medicine is available on the European Medicines Agency web site: https://www.ema.europa.eu.

Package leaflet: Information for the user

Humalog Mix50 100 units/ml KwikPen suspension for injection in a pre-filled pen
insulin lispro
Each KwikPen delivers 1 – 60 units in steps of 1 units.

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Humalog Mix50 KwikPen is and what it is used for
2. What you need to know before you use Humalog Mix50 KwikPen
3. How to use Humalog Mix50 KwikPen
4. Possible side effects
5. How to store Humalog Mix50 KwikPen
6. Contents of the pack and other information

1. What Humalog Mix50 KwikPen is and what it is used for

Humalog Mix50 KwikPen is used to treat diabetes. It is a premixed suspension. Its active substance is insulin lispro. 50% of the insulin lispro in Humalog Mix50 KwikPen is dissolved in water and it works more quickly than normal human insulin because the insulin molecule has been changed slightly. 50% of the insulin lispro in Humalog Mix50 KwikPen is available in a suspension together with protamine sulphate, so that its action is prolonged.

You get diabetes if your pancreas does not make enough insulin to control the level of glucose in your blood. Humalog Mix50 is a substitute for your own insulin and is used to control glucose in the long term. Humalog Mix50 works very quickly and longer than soluble insulin. You should normally use Humalog Mix50 within 15 minutes of a meal.

Your doctor may tell you to use Humalog Mix50 KwikPen as well as a longer-acting insulin. Each kind of insulin comes with another patient information leaflet to tell you about it. Do not change your insulin unless your doctor tells you to. Be very careful if you do change insulin.

The KwikPen is a disposable pre-filled pen containing 3 ml (300 units, 100 units/ml) of insulin lispro. One KwikPen contains multiple doses of insulin. The KwikPen dials 1 unit at a time. **The number of units are displayed in the dose window, always check this before your injection.** You can give from 1 to 60 units in a single injection. **If your dose is more than 60 units, you will need to give yourself more than one injection.**

2. What you need to know before you use Humalog Mix50 KwikPen

Do NOT use Humalog Mix50 KwikPen
- if you think **hypoglycaemia** (low blood sugar) is starting. Further in this leaflet it tells you how to deal with mild hypoglycaemia (see Section 3: If you take more Humalog Mix50 than you need).
- if you are **allergic** to insulin lispro or any of the other ingredients of this medicine (listed in section 6).

Warnings and precautions

- Always check the pack and the label of the pre-filled pen for the name and type of the insulin when you get it from your pharmacy. Make sure you get the Humalog Mix50 KwikPen that your doctor has told you to use.
- If your blood sugar levels are well controlled by your current insulin therapy, you may not feel the warning symptoms when your blood sugar is falling too low. Warning signs are listed later in this leaflet. You must think carefully about when to have your meals, how often to exercise and how much to do. You must also keep a close watch on your blood sugar levels by testing your blood glucose often.
- A few people who have had hypoglycaemia after switching from animal insulin to human insulin have reported that the early warning symptoms were less obvious or different. If you often have hypoglycaemia or have difficulty recognising them, please discuss this with your doctor.
- If you answer YES to any of the following questions, tell your doctor, pharmacist or diabetes nurse
  - Have you recently become ill?
  - Do you have trouble with your kidneys or liver?
  - Are you exercising more than usual?
- The amount of insulin you need may also change if you drink alcohol.
- You should also tell your doctor, pharmacist or diabetes nurse if you are planning to go abroad. The time difference between countries may mean that you have to have your injections and meals at different times from when you are at home.
- Some patients with long-standing type 2 diabetes mellitus and heart disease or previous stroke who were treated with pioglitazone and insulin experienced the development of heart failure. Inform your doctor as soon as possible, if you experience signs of heart failure such as unusual shortness of breath or rapid increase in weight or localised swelling (oedema).
- This Pen is not recommended for use by the blind or visually impaired without the help of someone trained to use the Pen.

Skin changes at the injection site

The injection site should be rotated to prevent skin changes such as lumps under the skin. The insulin may not work very well if you inject into a lumpy area (See How to use Humalog Mix50 KwikPen). Contact your doctor if you are currently injecting into a lumpy area before you start injecting a different area. Your doctor may tell you to check your blood sugar more closely, and to adjust your insulin or your other antidiabetic medications dose.

Other medicines and Humalog Mix50 KwikPen

Your insulin needs may change if you are taking

- the contraceptive pill,
- steroids,
- thyroid hormone replacement therapy,
- oral hypoglycaemics,
- acetyl salicylic acid,
- sulpha antibiotics,
- octreotide,
- "beta$_2$ stimulants" (for example ritodrine, salbutamol or terbutaline),
- beta-blockers, or
- some antidepressants (monoamine oxidase inhibitors or selective serotonin reuptake inhibitors),
- danazol,
- some angiotensin converting enzyme (ACE) inhibitors (for example captopril, enalapril), and
- angiotensin II receptor blockers.

Please tell your doctor, if you are taking, have recently taken or might take any other medicines, including medicines obtained without a prescription (see section "Warnings and precautions").

Pregnancy and breast-feeding
Are you pregnant or thinking about becoming pregnant, or are you breast-feeding? The amount of insulin you need usually falls during the first three months of pregnancy and increases for the remaining six months. If you are breast-feeding, you may need to alter your insulin intake or diet. Ask your doctor for advice.

Driving and using machines
Your ability to concentrate and react may be reduced if you have hypoglycaemia. Please keep this possible problem in mind in all situations where you might put yourself and others at risk (e.g. driving a car or operating machinery). You should contact your doctor about the advisability of driving if you have:

- frequent episodes of hypoglycaemia
- reduced or absent warning signs of hypoglycaemia

Humalog Mix50 KwikPen contains sodium
This medicine contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially 'sodium-free'.

3. How to use Humalog Mix50 KwikPen

Always use Humalog Mix50 KwikPen exactly as your doctor has told you. You should check with your doctor if you are not sure. To prevent the possible transmission of disease, each pen must be used by you only, even if the needle is changed.

Dose

- You should normally inject Humalog Mix50 within 15 minutes of a meal. If you need to, you can inject soon after a meal. But your doctor will have told you exactly how much to use, when to use it, and how often. These instructions are only for you. Follow them exactly and visit your diabetes clinic regularly.
- If you change the type of insulin you use (for example from a human or animal insulin to a Humalog product), you may have to take more or less than before. This might just be for the first injection or it may be a gradual change over several weeks or months.
- Humalog Mix50 KwikPen is only suitable for injecting just under the skin. Speak to your doctor if you need to inject your insulin by another method.

Preparing Humalog Mix50 KwikPen

- The KwikPen should be rotated in the palms of the hands ten times and inverted 180° ten times immediately before use to resuspend insulin until it appears uniformly cloudy or milky. If not, repeat the above procedure until contents are mixed. Cartridges contain a small glass bead to assist mixing. Do not shake vigorously as this may cause frothing which may interfere with the correct measurement of the dose. The cartridges should be examined frequently and should not be used if clumps of material are present or if solid white particles stick to the bottom or wall of the cartridge, giving it a frosted appearance. Check each time you inject yourself.

Getting the KwikPen ready to use (Please see user manual)

- First wash your hands.
- Read the instructions on how to use your pre-filled insulin pen. Please follow the instructions carefully. Here are some reminders.
- Use a clean needle. (Needles are not included).
- Prime your KwikPen before each use. This checks that insulin comes out and clears the air bubbles from your KwikPen. There may still be some small air bubbles left in the pen - these are harmless. But if the air bubbles are too large it may affect the insulin dose.

Injecting Humalog Mix50

- Before you make an injection, clean your skin as you have been instructed. Inject under the skin, as you were taught. Do not inject directly into a vein. After your injection, leave the

needle in the skin for five seconds to make sure you have taken the whole dose. Do not rub the area you have just injected. Make sure you inject at least half an inch (1 cm) from where you last injected and that you 'rotate' the places you inject, as you have been taught.

After injecting

- As soon as you have done the injection, unscrew the needle from the KwikPen using the outer needle cap. This will keep the insulin sterile and stop it leaking. It also stops air entering the pen and your needle clogging**. Do not share your needles**. Do not share your pen. Replace the cap on the pen.

Further injections

- Every time you use a KwikPen you must use a new needle. Before every injection, clear any air bubbles. You can see how much insulin is left by holding the KwikPen with the needle pointing up. The scale on the cartridge shows about how many units you have left.
- Do not mix any other insulin in your disposable pen. Once the KwikPen is empty, do not use it again. Please get rid of it carefully - your pharmacist or diabetes nurse will tell you how to do this.

If you use more Humalog Mix50 than you need

If you use more Humalog Mix50 than you need or are unsure how much you have injected, a low blood sugar may occur. Check your blood sugar.

If your blood sugar is low **(mild hypoglycaemia)**, eat glucose tablets, sugar or drink a sugary drink. Then eat fruit, biscuits, or a sandwich, as your doctor has advised you and have some rest. This will often get you over mild hypoglycaemia or a minor insulin overdose. If you get worse and your breathing is shallow and your skin gets pale, tell your doctor at once. A glucagon injection can treat quite severe hypoglycaemia. Eat glucose or sugar after the glucagon injection. If you do not respond to glucagon, you will have to go to hospital. Ask your doctor to tell you about glucagon.

If you forget to use Humalog Mix50

If you take less Humalog Mix50 than you need, a high blood sugar may occur. Check your blood sugar

If hypoglycaemia (low blood sugar) or hyperglycaemia (high blood sugar) is not treated they can be very serious and cause headaches, nausea, vomiting, dehydration, unconsciousness, coma or even death (see A and B in section 4 "Possible Side Effects").

Three simple steps to avoid hypoglycaemia or hyperglycaemia are:

- Always keep a spare pen and cartridges, in case you lose your KwikPen or it gets damaged.
- Always carry something to show you are diabetic.
- Always carry sugar with you.

If you stop using Humalog Mix50.

If you take less Humalog Mix50 than you need, a high blood sugar may occur. Do not change your insulin unless your doctor tells you to.

If you have any further questions on the use of this product, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Systemic allergy is rare (≥ 1/10,000 to <1/1,000). The symptoms are as follows:

- rash over the whole body
- difficulty in breathing
- wheezing
- blood pressure dropping
- heart beating fast
- sweating

If you think you are having this sort of insulin allergy with Humalog Mix50, tell your doctor at once.

Local allergy is common (≥ 1/100 to <1/10). Some people get redness, swelling or itching around the area of the insulin injection. This usually clears up in anything from a few days to a few weeks. If this happens to you, tell your doctor.

Lipodystrophy is uncommon (≥ 1/1,000 to <1/100). If you inject insulin too often at the same place, the fatty tissue may either shrink (lipoatrophy) or thicken (lipohypertrophy). Lumps under the skin may also be caused by build-up of a protein called amyloid (cutaneous amyloidosis). The insulin may not work very well if you inject into a lumpy area. Change the injection site with each injection to help prevent these skin changes.

Oedema (e.g. swelling in arms, ankles; fluid retention) has been reported, particularly at the start of insulin therapy or during a change in therapy to improve control of your blood glucose.

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

Common problems of diabetes

A. Hypoglycaemia
Hypoglycaemia (low blood sugar) means there is not enough sugar in the blood. This can be caused if:
- you take too much Humalog Mix50 or other insulin;
- you miss or delay meals or change your diet;
- you exercise or work too hard just before or after a meal;
- you have an infection or illness (especially diarrhoea or vomiting);
- there is a change in your need for insulin; or
- you have trouble with your kidneys or liver which gets worse.

Alcohol and some medicines can affect your blood sugar levels.

The first symptoms of low blood sugar usually come on quickly and include the following:
- tiredness
- nervousness or shakiness
- headache
- rapid heartbeat
- feeling sick
- cold sweat

While you are not confident about recognising your warning symptoms, avoid situations, e.g. driving a car, in which you or others would be put at risk by hypoglycaemia.

B. Hyperglycaemia and diabetic ketoacidosis
Hyperglycaemia (too much sugar in the blood) means that your body does not have enough insulin. Hyperglycaemia can be brought about by:
- not taking your Humalog or other insulin;
- taking less insulin than your doctor tells you to;
- eating a lot more than your diet allows; or
- fever, infection or emotional stress.

Hyperglycaemia can lead to diabetic ketoacidosis. The first symptoms come on slowly over many hours or days. The symptoms include the following:
- feeling sleepy
- flushed face
- thirst
- no appetite
- fruity smell on the breath
- feeling or being sick

Severe symptoms are heavy breathing and a rapid pulse. **Get medical help immediately.**

C. Illness
If you are ill, especially if you feel sick or are sick, the amount of insulin you need may change. **Even when you are not eating normally, you still need insulin.** Test your urine or blood, follow your 'sick rules', and tell your doctor.

5. How to store Humalog Mix50 KwikPen

Before the first use store your Humalog Mix50 KwikPen in a refrigerator (2°C – 8°C). Do not freeze.

Keep your Humalog Mix50 KwikPen in use at room temperature (below 30°C) and discard after 28 days. Do not put it near heat or in the sun. Do not keep the KwikPen that you are using in the fridge. The KwikPen should not be stored with the needle attached.

Keep out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the label and the carton. The expiry date refers to the last day of that month.

Do not use this medicine if you notice clumps of material are present or if solid white particles stick to the bottom or wall of the cartridge, giving it a frosted appearance. Check each time you inject yourself.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. Contents of the pack and other information

What Humalog Mix50 100 units/ml KwikPen suspension for injection contains
- The active substance is insulin lispro. Insulin lispro is made in the laboratory by a 'recombinant DNA technology' process. It is a changed form of human insulin and so is different from other human and animal insulins. Insulin lispro is closely related to human insulin which is a natural hormone made by the pancreas.
- The other ingredients are protamine sulphate, m-cresol, phenol, glycerol, dibasic sodium phosphate $7H_2O$, zinc oxide and water for injection. Sodium hydroxide or hydrochloric acid may have been used to adjust the acidity.

What Humalog Mix50 100 units/ml KwikPen suspension for injection looks like and contents of the pack
Humalog Mix50 100 units/ml KwikPen suspension for injection is a white, sterile suspension and contains 100 units of insulin lispro in each millilitre (100 units/ml) suspension for injection. 50% of the insulin lispro in Humalog Mix50 is dissolved in water. 50% of the insulin lispro in Humalog Mix50 is available in a suspension together with protamine sulphate. Each Humalog Mix50 KwikPen contains 300 units (3 millilitres). The Humalog Mix50 KwikPen comes in a pack of 5 pre-filled pens or a multipack of 2 x 5 pre-filled pens. Not all pack sizes may be marketed. The Humalog Mix50 in your KwikPen is the same as the Humalog Mix50, which comes in separate Humalog Mix50 cartridges. The KwikPen simply has a built in cartridge. When the KwikPen is empty you cannot use it again.

Marketing Authorisation Holder and Manufacturer
Humalog Mix50 100 units/ml KwikPen suspension for injection is made by:
- Lilly France S.A.S., Rue du Colonel Lilly, 67640 Fegersheim, France,
- Eli Lilly Italia S.p.A., Via Gramsci 731-733, 50019 Sesto Fiorentino, (FI) Italy.

The product licence is held by: Eli Lilly Nederland B.V., Orteliuslaan 1000, 3528 BD Utrecht, The Netherlands.

For any information about this medicinal product, please contact the local representative of the Marketing Authorisation Holder:

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This leaflet was last revised in {MM/YYYY}.

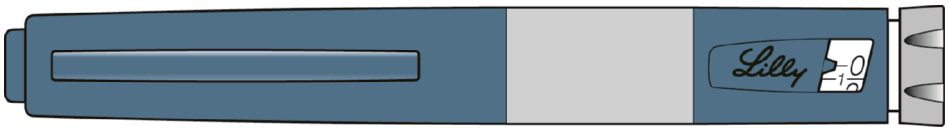
USER MANUAL

Please see manual text later.

Detailed information on this medicine is available on the European Medicines Agency web site: https://www.ema.europa.eu.

USER MANUAL
KwikPen pre-filled insulin pen

100 units/ml



PLEASE READ THIS USER MANUAL BEFORE USE

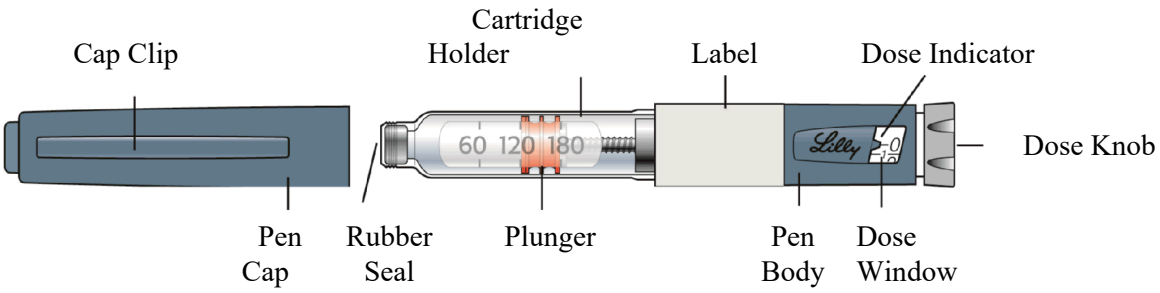
Read the User Manual before you start taking your insulin and each time you get another KwikPen. There may be new information. This information does not take the place of talking to your healthcare professional about your medical condition or your treatment.

KwikPen ("Pen") is a disposable pre-filled pen containing 3 ml (300 units, 100 units/ml) of insulin. You can give yourself multiple doses using one Pen. The Pen dials 1 unit at a time. You can give from 1 to 60 units in a single injection. **If your dose is more than 60 units, you will need to give yourself more than one injection.** The plunger only moves a little with each injection, and you may not notice that it moves. The plunger will only reach the end of the cartridge when you have used all 300 units in the Pen.

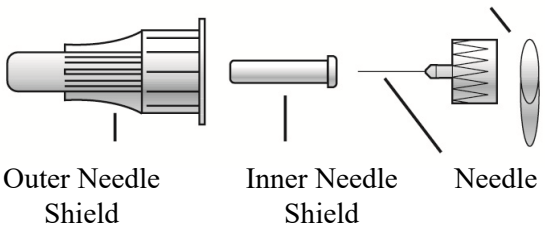
Do not share your pen with other people, even if the needle has been changed. Do not reuse or share needles with other people. You may give an infection to them or get an infection from them.

This Pen is not recommended for use by the blind or visually impaired without the help of someone trained to use the Pen.

KwikPen Parts



Pen Needle Parts
(Needles Not Included)



How to recognize your KwikPen:

	Humalog Solution	**Humalog Mix25** Suspension (cloudy insulin)	**Humalog Mix50** Suspension (cloudy insulin)
Pen colour:	Blue	Blue	Blue
Dose Knob:	Burgundy	Yellow	Red
Labels:	White with Burgundy Colour Bar	White with Yellow Colour Bar	White with Red Colour Bar

Supplies needed to give your injection:

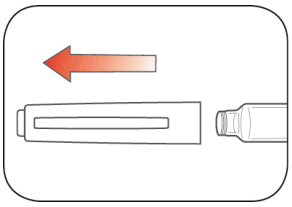
- KwikPen containing your insulin
- KwikPen compatible Needle (BD [Becton, Dickinson and Company] Pen Needles recommended)
- Swab

Needles and swab are not included.

Preparing your Pen

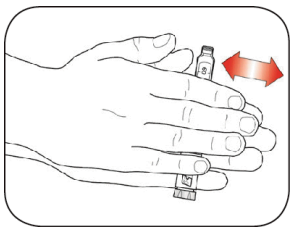
- Wash your hands with soap and water.
- Check the Pen to make sure you are taking the right type of insulin. This is especially important if you use more than 1 type of insulin.
- **Do not** use your Pen past the expiration date printed on the Label. After you start using the Pen, throw your Pen away after the in-use time specified in the Package Leaflet.
- Always use a **new Needle** for each injection to help prevent infections and blocked Needles.

Step 1:



- Pull the Pen Cap straight off.
  - **Do not** remove the Pen Label.
- Wipe the Rubber Seal with a swab.

Step 2:

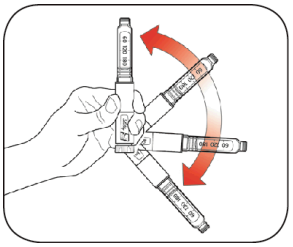


(For HUMALOG suspensions cloudy insulins only)

- Gently roll the Pen 10 times.

AND

- Invert the Pen 10 times.

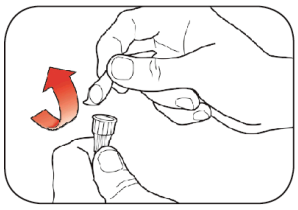


Mixing is important to make sure you get the right dose.
The insulin should look evenly mixed.

Step 3:

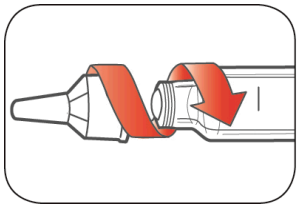
- Check the appearance of the insulin.
  - HUMALOG solution should look clear and colourless. Do not use if it is cloudy, coloured, or has particles or clumps in it.
  - HUMALOG suspensions - cloudy insulins - should look white after mixing. **Do not** use if it looks clear or contains any clumps or particles.

Step 4:



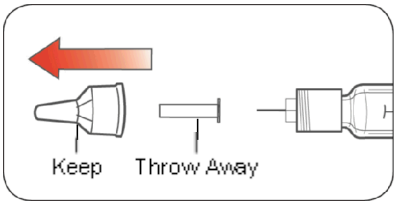
- Select a new Needle.
- Pull off the Paper Tab from the Outer Needle Shield.

Step 5:



- Push the capped Needle straight onto the Pen and twist the Needle on until it is tight.

Step 6:



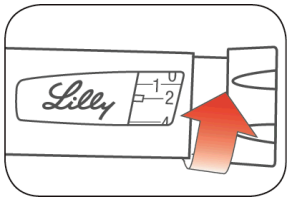
- Pull off the Outer Needle Shield. **Do not** throw it away.
- Pull off the Inner Needle Shield and throw it away.

Priming your Pen
Prime before each injection.

- Priming your Pen means removing the air from the Needle and Cartridge that may collect during normal use and ensures that the Pen is working correctly.
- If you **do not** prime before each injection, you may get too much or too little insulin.

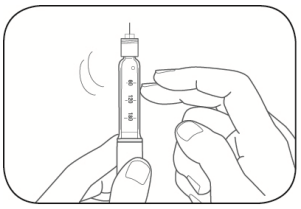
Step 7:

- To prime your Pen, turn the Dose Knob to select 2 units.



Step 8:

- Hold your Pen with the Needle pointing up. Tap the Cartridge Holder gently to collect air bubbles at the top



Step 9:

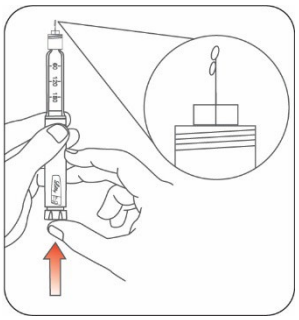
- Continue holding your Pen with Needle pointing up. Push the Dose Knob in until it stops, and "0" is seen in the Dose Window. Hold the Dose Knob in and count to 5 slowly.

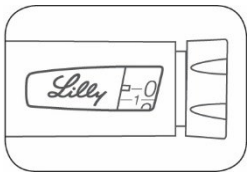
  You should see insulin at the tip of the Needle.

  – If you **do not** see insulin, repeat the priming steps, but not more than 4 times.

  – If you **still do not** see insulin, change the Needle and repeat the priming steps.

  Small air bubbles are normal and will not affect your dose.



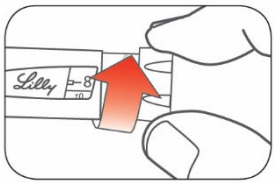


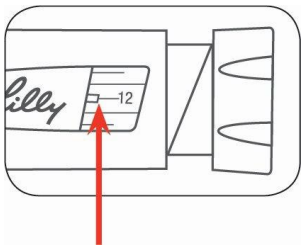
Selecting your dose

- You can give from 1 to 60 units in a single injection.
- If your dose is more than 60 units, you will need to give more than one injection.
  – If you need help deciding how to divide up your dose, ask your healthcare professional.
  – You should use a new Needle for each injection and repeat the priming step.

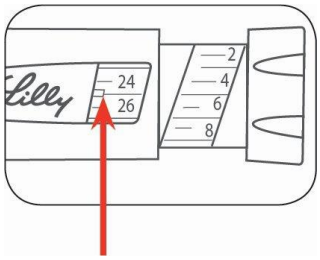
Step 10:

- Turn the Dose Knob to select the number of units you need to inject. The Dose Indicator should line up with your dose.
  - The Pen dials 1 unit at a time.
  - The Dose Knob clicks as you turn it.
  - **DO NOT** dial your dose by counting the clicks because you may dial the wrong dose.
  - The dose can be corrected by turning the Dose Knob in either direction until the correct dose lines up with the Dose Indicator.
  - The even numbers are printed on the dial.
  - The odd numbers, after the number 1, are shown as full lines.





(Example: 12 units shown in the Dose Window)



(Example: 25 units shown in the Dose Window)

- **Always check the number in the Dose Window to make sure you have dialled the correct dose.**

- The Pen will not let you dial more than the number of units left in the Pen.
- If you need to inject more than the number of units left in the Pen, you may either:
  - inject the amount left in your Pen and then use a new Pen to give the rest of your dose, **or**
  - get a new Pen and inject the full dose.
- It is normal to see a small amount of insulin left in the Pen that you cannot inject.

Giving your injection

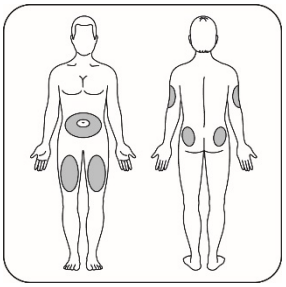
- Inject your insulin as your healthcare professional has shown you.
- Change (rotate) your injection site for each injection.
- **Do not** try to change your dose while injecting.

Step 11:

- Choose your injection site.

  Your insulin is injected under the skin (subcutaneously) of your stomach area, buttocks, upper legs or upper arms.

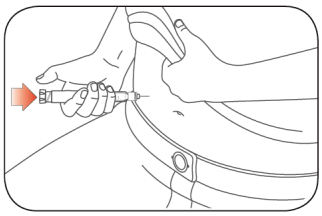
- Wipe your skin with a swab, and let the injection site dry before you inject your dose.



Step 12:

- Insert the Needle into your skin.
- Push the Dose Knob all the way in.
- Continue to hold the Dose Knob in and **slowly count to 5** before removing the Needle.

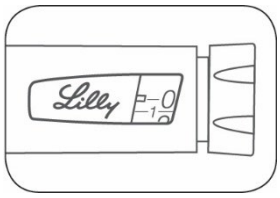




Do not try to inject your insulin by turning the Dose Knob. You will **NOT** receive your insulin by turning the Dose Knob.

Step 13:

- Pull the Needle out of your skin.
  - A drop of insulin at the Needle tip is normal. It will not affect your dose.
- Check the number in the Dose Window
  - If you see “0” in the Dose window, you have received the full amount you dialled.
  - If you do not see “0” in the Dose window, do not redial. Insert the needle into your skin and finish your injection.
  - If you **still** do not think you received the full amount you dialled for your injection**, do not start over or repeat that injection.** Monitor your blood glucose as instructed by your healthcare professional.
  - If you normally need to give 2 injections for your full dose, be sure to give your second injection.



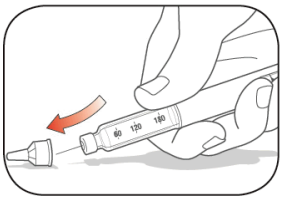
The plunger only moves a little with each injection, and you may not notice that it moves.

If you see blood after you take the Needle out of your skin, press the injection site lightly with a piece of gauze or a swab. **Do not** rub the area.

After your injection

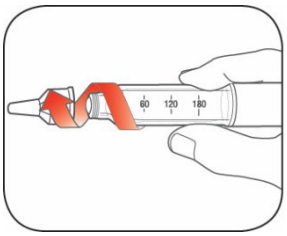
Step 14:

- Carefully replace the Outer Needle Shield.



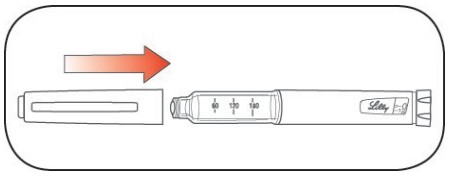
Step 15:

- Unscrew the capped Needle and dispose of it as described below (see **Disposing of Pens and Needles** section).
- Do not store the Pen with the Needle attached to prevent leaking, blocking the Needle, and air from entering the Pen.



Step 16:

- Replace the Pen Cap by lining up the Cap Clip with the Dose Indicator and pushing straight on.



Disposing of pens and needles

- Put used Needles in a sharps container or a hard plastic container with a secure lid. **Do not** throw needles directly into your household waste.
- **Do not** recycle the filled sharps container.
- Ask your healthcare professional about options to dispose of the Pen and the sharps container properly.
- The directions regarding needle handling are not intended to replace local, healthcare professional or institutional policies.

Storing your pen

Unused pens

- Store unused Pens in the refrigerator at 2°C to 8°C.
- **Do not** freeze your insulin. **Do not** use if it has been frozen.
- Unused Pens may be used until the expiration date printed on the Label, if the Pen has been kept in the refrigerator.

In-use Pen

- Store the Pen you are currently using at room temperature (below 30°C) and away from dust, food and liquids, heat and light.
- Throw away the Pen you are using after the time specified in the Package Leaflet, even if it still has insulin left in it.

General information about the safe and effective use of your pen

- **Keep your Pen and Needles out of the sight and reach of children.**
- **Do not** use your Pen if any part looks broken or damaged.
- Always carry an extra Pen in case yours is lost or damaged.

Troubleshooting

- If you cannot remove the Pen Cap, gently twist the cap back and forth, and then pull the cap straight off.
- If the Dose Knob is hard to push:
  - Pushing the Dose Knob more slowly will make it easier to inject.
  - Your Needle may be blocked. Put on a new Needle and prime the Pen.
  - You may have dust, food, or liquid inside the Pen. Throw the Pen away and get a new Pen. You may need to get a prescription from your healthcare professional.

If you have any questions or problems with your KwikPen, call your healthcare professional for help or contact your local Lilly affiliate

Document Revision Date:

Package leaflet: Information for the user

Humalog 200 units/ml KwikPen solution for injection in a pre-filled pen
insulin lispro
Each KwikPen delivers 1 – 60 units in steps of 1 units.

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Humalog 200 units/ml KwikPen is and what it is used for
2. What you need to know before you use Humalog 200 units/ml KwikPen
3. How to use Humalog 200 units/ml KwikPen
4. Possible side effects
5. How to store Humalog 200 units/ml KwikPen
6. Contents of the pack and other information

1. What Humalog 200 units/ml KwikPen is and what it is used for

Humalog 200 units/ml KwikPen is used to treat diabetes. Humalog works more quickly than normal human insulin because insulin lispro has been changed slightly in comparison to human insulin. Insulin lispro is closely related to human insulin which is a natural hormone made by the pancreas.

You get diabetes if your pancreas does not make enough insulin to control the level of glucose in your blood. Humalog is a substitute for your own insulin and is used to control glucose in the long term. It works very quickly and lasts a shorter time than soluble insulin (2 to 5 hours). You should normally use Humalog within 15 minutes of a meal.

Your doctor may tell you to use Humalog 200 units/ml KwikPen as well as a longer-acting insulin. Each kind of insulin comes with another patient information leaflet to tell you about it. Do not change your insulin unless your doctor tells you to.

Humalog 200 units/ml KwikPen should be reserved for the treatment of adults with diabetes requiring daily doses of more than 20 units of rapid-acting insulin.

Humalog 200 units/ml KwikPen is a disposable pre-filled pen containing 3 ml (600 units, 200 units/ml) of insulin lispro. One KwikPen contains multiple doses of insulin. The KwikPen dials 1 unit at a time. **The number of units are displayed in the dose window, always check this before your injection.** You can give from 1 to 60 units in a single injection. **If your dose is more than 60 units, you will need to give yourself more than one injection.**

2. What you need to know before you use Humalog 200 units/ml KwikPen

Do NOT use Humalog 200 units/ml KwikPen
- if you are **allergic** to insulin lispro or any of the other ingredients of this medicine (listed in section 6).
- if you think **hypoglycaemia** (low blood sugar) is starting. Further in this leaflet it tells you how to deal with mild hypoglycaemia (see section 3: If you use more Humalog than you should).

Warnings and precautions

- Always check the pack and the label of the pre-filled pen for the name and type of the insulin when you get it from your pharmacy. Make sure you get the Humalog 200 units/ml KwikPen that your doctor has told you to use.
- **The Humalog 200 units/ml solution for injection in your pre-filled pen (the KwikPen) should ONLY be injected with this pre-filled pen. Do not transfer the insulin lispro from your Humalog 200 units/ml KwikPen to a syringe**. The markings on the insulin syringe will not measure your dose correctly. A severe overdose can result, causing low blood sugar which may put your life in danger. Do not transfer insulin from your Humalog 200 units/ml KwikPen to any other insulin delivery devices like insulin infusion pumps.
- **Do NOT mix the Humalog 200 units/ml solution for injection in your pre-filled pen (the KwikPen) with any other insulin or any other medicine.** The Humalog 200 units/ml solution for injection should not be diluted.
- If your blood sugar levels are well controlled by your current insulin therapy, you may not feel the warning symptoms when your blood sugar is falling too low. Warning signs are listed in section 4 of this leaflet. You must think carefully about when to have your meals, how often to exercise and how much to do. You must also keep a close watch on your blood sugar levels by testing your blood glucose often.
- A few people who have had hypoglycaemia after switching from animal insulin to human insulin have reported that the early warning symptoms were less obvious or different. If you often have hypoglycaemia or have difficulty recognising it, please discuss this with your doctor.
- If you answer YES to any of the following questions, tell your doctor, pharmacist or diabetes nurse
  - Have you recently become ill?
  - Do you have trouble with your kidneys or liver?
  - Are you exercising more than usual?
- You should also tell your doctor, pharmacist or diabetes nurse if you are planning to go abroad. The time difference between countries may mean that you have to have your injections and meals at different times from when you are at home.
- Some patients with long-standing type 2 diabetes mellitus and heart disease or previous stroke who were treated with pioglitazone and insulin experienced the development of heart failure. Inform your doctor as soon as possible, if you experience signs of heart failure such as unusual shortness of breath or rapid increase in weight or localised swelling (oedema).
- This Pen is not recommended for use by the blind or visually impaired without the help of someone trained to use the Pen.

Skin changes at the injection site

The injection site should be rotated to prevent skin changes such as lumps under the skin. The insulin may not work very well if you inject into a lumpy area (See How to use Humalog 200 units/ml KwikPen). Contact your doctor if you are currently injecting into a lumpy area before you start injecting a different area. Your doctor may tell you to check your blood sugar more closely, and to adjust your insulin or your other antidiabetic medications dose.

Other medicines and Humalog 200 units/ml KwikPen

Your insulin needs may change if you are taking

- the contraceptive pill,
- steroids,
- thyroid hormone replacement therapy,
- oral hypoglycaemics, (e.g. metformin, acarbose, sulphonylurea agents, pioglitazone, empagliflozin, DPP-4-inhibitors like sitagliptin or saxagliptine,),
- acetyl salicylic acid,
- sulpha antibiotics,
- somatostatin analogues (such as octreotide, used to treat an uncommon condition in which you make too much growth hormone),

- "beta$_2$ stimulants"such as salbutamol or terbutaline to treat asthma, or ritodrine used to stop premature labor,
- beta-blockers – to treat high blood pressure., or
- some antidepressants (monoamine oxidase inhibitors or selective serotonin reuptake inhibitors),
- danazol (medicine acting on ovulation),
- some angiotensin converting (ACE) inhibitors, used to treat certain heart conditions or high blood pressure (for example captopril, enalapril), and
- specific medicines to treat high blood pressure, kidney damage due to diabetes, and some heart problems (angiotensin II receptor blockers).

Please tell your doctor, if you are taking, have recently taken or might take any other medicines. (see also section "Warnings and precautions").

Humalog with alcohol

Your blood sugar levels may either rise or fall if you drink alcohol. Therefore the amount of insulin needed may change.

Pregnancy and breast-feeding
Are you pregnant or thinking about becoming pregnant, or are you breast-feeding? The amount of insulin you need usually falls during the first three months of pregnancy and increases for the remaining six months. If you are breast-feeding, you may need to alter your insulin intake or diet. Ask your doctor for advice.

Driving and using machines
Your ability to concentrate and react may be reduced if you have hypoglycaemia. Please keep this possible problem in mind in all situations where you might put yourself and others at risk (e.g. driving a car or using machines). You should contact your doctor about the advisability of driving if you have:
- frequent episodes of hypoglycaemia
- reduced or absent warning signs of hypoglycaemia

Humalog 200 units/ml KwikPen contains sodium
This medicine contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially 'sodium-free'.

3. How to use Humalog 200 units/ml KwikPen

Always use this medicine exactly as your doctor has told you. You should check with your doctor if you are not sure. To prevent the possible transmission of disease, each pen must be used by you only, even if the needle is changed.

Humalog 200 units/ml KwikPen is for patients taking more than 20 units of rapid-acting insulin a day.

Do not transfer insulin from your Humalog 200 units/ml KwikPen to a syringe. The markings on the insulin syringe will not measure your dose correctly. A severe overdose can result, causing low blood sugar which may put your life in danger.

Do not use Humalog 200 units/ml KwikPen solution for injection in an insulin infusion pump.

Dose
- You should normally inject Humalog within 15 minutes of a meal. If you need to, you can inject soon after a meal. But your doctor will have told you exactly how much to use, when to use it, and how often. These instructions are only for you. Follow them exactly and visit your diabetes clinic regularly.

- If you change the type of insulin you use (for example from a human or animal insulin to a Humalog product), you may have to take more or less than before. This might just be for the first injection or it may be a gradual change over several weeks or months.
- Inject Humalog under the skin (subcutaneously).

Preparing Humalog 200 units/ml KwikPen
- Humalog is already dissolved in water, so you do not need to mix it. But you must use it **only** if it looks like water. It must be clear, have no colour and no solid pieces in it. Check each time you inject yourself.

Getting the KwikPen ready to use (Please see user manual)
- First wash your hands.
- Read the instructions on how to use your pre-filled insulin pen. Please follow the instructions carefully. Here are some reminders.
- Use a clean needle. (Needles are not included).
- Prime your KwikPen before each use. This checks that insulin comes out and clears the air bubbles from your KwikPen. There may still be some small air bubbles left in the pen - these are harmless. But if the air bubbles are too large it may affect the insulin dose.

Injecting Humalog
- Before you make an injection, clean your skin as you have been instructed. Inject under the skin, as you were taught. After your injection, leave the needle in the skin for five seconds to make sure you have taken the whole dose. Do not rub the area you have just injected. Make sure you inject at least half an inch (1 cm) from the last injection and that you 'rotate' the places you inject, as you have been taught. It doesn't matter which injection site you use, either upper arm, thigh, buttock or abdomen, your Humalog injection will still work quicker than soluble human insulin.
- Do not inject Humalog 200 units/ml KwikPen solution for injection directly into a vein (intravenously).

After injecting
- As soon as you have done the injection, unscrew the needle from the KwikPen using the outer needle cap. This will keep the insulin sterile and stop it leaking. It also stops air entering the pen and your needle clogging. **Do not share your needles**. Do not share your pen. Replace the cap on your pen.

Further injections
- Every time you use a KwikPen you must use a new needle. Before every injection, clear any air bubbles. You can see how much insulin is left by holding the KwikPen with the needle pointing up.
- Once the KwikPen is empty, do not use it again. Please get rid of it carefully - your pharmacist or diabetes nurse will tell you how to do this.

If you use more Humalog than should
If you use more Humalog than you need or are unsure how much you have injected, a low blood sugar may occur. Check your blood sugar.

If your blood sugar is low **(mild hypoglycaemia)**, eat glucose tablets, sugar or drink a sugary drink. Then eat fruit, biscuits, or a sandwich, as your doctor has advised you and have some rest. This will often get you over mild hypoglycaemia or a minor insulin overdose. If you get worse and your breathing is shallow and your skin gets pale, tell your doctor at once. A glucagon injection can treat quite severe hypoglycaemia. Eat glucose or sugar after the glucagon injection. If you do not respond to glucagon, you will have to go to hospital. Ask your doctor to tell you about glucagon.

If you forget to use Humalog
If you take less Humalog than you need or are unsure how much you have injected, a high blood sugar may occur. Check your blood sugar

If hypoglycaemia (low blood sugar) or hyperglycaemia (high blood sugar) is not treated, they can be very serious and cause headaches, feeling sick (nausea), being sick (vomiting), loss of fluids (dehydration), unconsciousness, coma or even death (see section 4 "Possible side effects").

Three simple steps to avoid hypoglycaemia or hyperglycaemia are:
- Always carry a spare pen in case you lose your KwikPen or it gets damaged.
- Always carry something to show you are diabetic.
- Always carry sugar with you.

If you stop using Humalog.
If you take less Humalog than you need, a high blood sugar may occur. Do not change your insulin unless your doctor tells you to.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Severe allergy is rare (may affect up to 1 in 1,000 people). The symptoms are as follows:
- rash over the whole body
- difficulty in breathing
- wheezing
- blood pressure dropping
- heart beating fast
- sweating

If you think you are having this sort of insulin allergy with Humalog, contact a doctor at once.

Local allergy is common (may affect up to 1 in 10 people). Some people get redness, swelling or itching around the area of the insulin injection. This usually clears up in anything from a few days to a few weeks. If this happens to you, tell your doctor.

Lipodystrophy is uncommon (may affect up to 1 in 100 people).. If you inject insulin too often at the same place, the fatty tissue may either shrink (lipoatrophy) or thicken (lipohypertrophy). Lumps under the skin may also be caused by build-up of a protein called amyloid (cutaneous amyloidosis). The insulin may not work very well if you inject into a lumpy area. Change the injection site with each injection to help prevent these skin changes.

Oedema (e.g. swelling in arms, ankles; fluid retention) has been reported, particularly at the start of insulin therapy or during a change in therapy to improve control of your blood glucose.

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

Common problems of diabetes

Hypoglycaemia
Hypoglycaemia (low blood sugar) means there is not enough sugar in the blood. This can be caused if:
- you take too much Humalog or other insulin;
- you miss or delay meals or change your diet;
- you exercise or work too hard just before or after a meal;
- you have an infection or illness (especially diarrhoea or vomiting);

- there is a change in your need for insulin; or
- you have trouble with your kidneys or liver which gets worse.

Alcohol and some medicines can affect your blood sugar levels (see section 2).

The first symptoms of low blood sugar usually come on quickly and include the following:
- tiredness
- nervousness or shakiness
- headache
- rapid heartbeat
- feeling sick
- cold sweat

While you are not confident about recognising your warning symptoms, avoid situations such as driving a car, in which you or others would be put at risk by hypoglycaemia.

Hyperglycaemia and diabetic ketoacidosis
Hyperglycaemia (too much sugar in the blood) means that your body does not have enough insulin. Hyperglycaemia can be brought about by:
- not taking your Humalog or other insulin;
- taking less insulin than your doctor tells you to;
- eating a lot more than your diet allows; or
- fever, infection or emotional stress.

Hyperglycaemia can lead to diabetic ketoacidosis. The first symptoms come on slowly over many hours or days. The symptoms include the following:
- feeling sleepy
- flushed face
- thirst
- no appetite
- fruity smell on the breath
- feeling or being sick

Severe symptoms are heavy breathing and a rapid pulse. **Get medical help immediately.**

Illness
If you are ill, especially if you feel sick or are sick, the amount of insulin you need may change. **Even when you are not eating normally, you still need insulin.** Test your urine or blood, follow your 'sick rules', and tell your doctor.

5. How to store Humalog 200 units/ml KwikPen

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the label and the carton. The expiry date refers to the last day of that month.

Before the first use store your Humalog **200 units/ml** KwikPen in a refrigerator (2°C – 8°C). Do not freeze.

Keep your Humalog **200 units/ml** KwikPen in use at room temperature (below 30°C) and discard after 28 days. Do not put it near heat or in the sun. Do not keep the KwikPen that you are using in the fridge. The KwikPen should not be stored with the needle attached.

Do not use this medicine if you notice the solution is coloured or it has solid pieces in it. You must use it **only** if it looks like water. Check this each time you inject yourself.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. Contents of the pack and other information

What Humalog 200 units/ml KwikPen solution for injection contains
- The active substance is insulin lispro. Each ml of solution contains 200 units (U) of insulin lispro. Each pre-filled pen (3 ml) contains 600 units (U) of insulin lispro.
- The other ingredients are metacresol, glycerol, trometamol, zinc oxide and water for injection. Sodium hydroxide or hydrochloric acid may have been used to adjust the acidity.

What Humalog 200 units/ml KwikPen looks like and contents of the pack
Humalog 200 units/ml KwikPen solution for injection is a sterile, clear, colourless, aqueous solution and contains 200 units of insulin lispro in each millilitre (200 units/ml) solution for injection. Each Humalog **200 units/ml** KwikPen contains 600 units (3 millilitres). The Humalog **200 units/ml** KwikPen comes in a pack of 1, 2 or 5 pre-filled pens or multipacks of 2 x 5 pre-filled pens. Not all pack sizes may be marketed. The KwikPen simply has a built in cartridge. When the pre-filled pen is empty you cannot use it again.

Marketing Authorisation Holder
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Manufacturer
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This leaflet was last revised in {MM/YYYY}.

USER MANUAL

Please see manual text later.

Detailed information on this medicine is available on the European Medicines Agency web site: https://www.ema.europa.eu.

USER MANUAL
Humalog 200 units/ml KwikPen solution for injection in a pre-filled pen

insulin lispro



PLEASE READ THIS USER MANUAL BEFORE USE



Read the User Manual before you start taking Humalog 200 units/ml KwikPen solution for injection and each time you get another Humalog 200 units/ml KwikPen. There may be new information. This information does not take the place of talking to your healthcare professional about your medical condition or your treatment.

Humalog 200 units/ml KwikPen ("Pen") is a disposable pre-filled pen containing 3 ml (600 units, 200 units/ml) of insulin lispro solution for injection. You can give yourself multiple doses using one Pen. The Pen dials 1 unit at a time. You can inject from 1 to 60 units in a single injection. **If your dose is more than 60 units, you will need to give yourself more than one injection.** The plunger only moves a little with each injection, and you may not notice that it moves. The plunger will only reach the end of the cartridge when you have used all 600 units in the Pen.

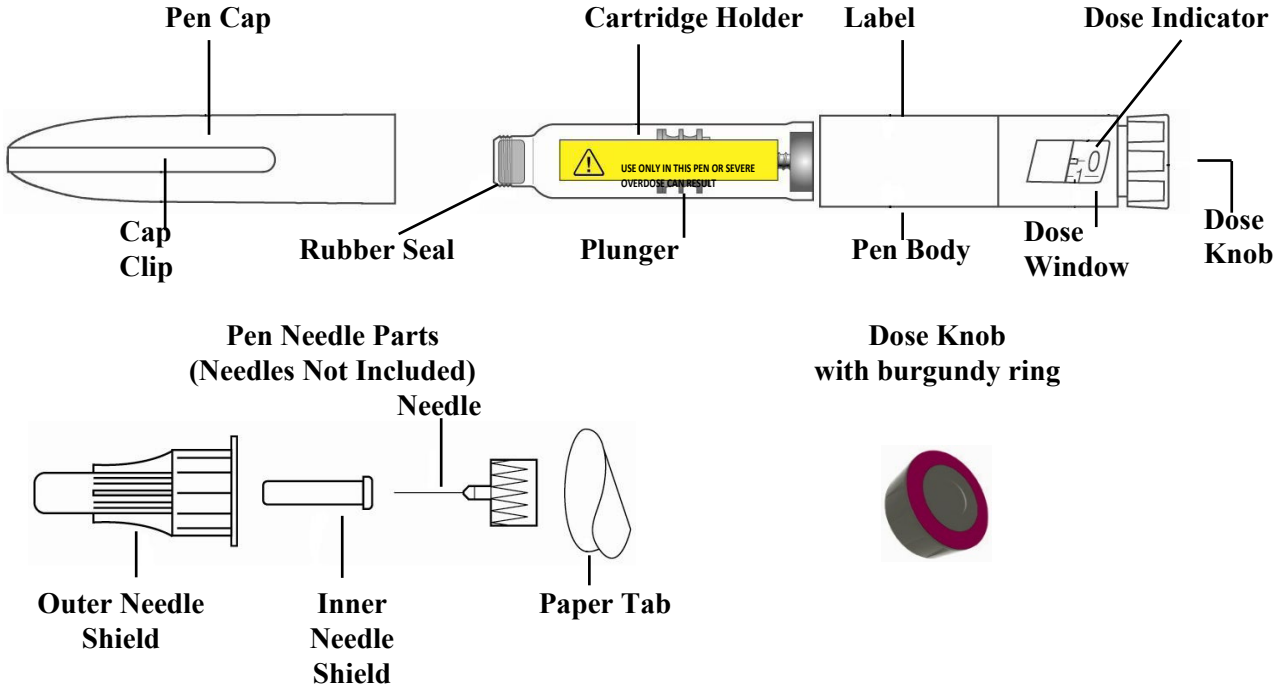
This pen is designed to allow you to give more doses than other pens you may have used in the past. Dial your usual dose as instructed by your healthcare professional.

Humalog KwikPen is available in two strengths, 100 units/ml and 200 units/ml. Inject Humalog 200 units/ml ONLY with your Pen. DO NOT transfer insulin from your Pen to another insulin delivery device. Syringes and insulin pumps will not dose 200 units/ml insulin correctly. A severe overdose can result, causing very low blood sugar which may put your life in danger.

Do not share your Pen with other people, even if the needle has been changed. Do not reuse or share needles with other people.. You may give an infection to them or get an infection from them.

This Pen is not recommended for use by the blind or visually impaired without the help of someone trained to use the Pen.

KwikPen Parts



How to recognize your Humalog 200 units/ml KwikPen:

- Pen colour: Dark grey
- Dose Knob: Dark grey with burgundy ring on the end
- Labels: Burgundy, “200 units/ml” in yellow box. Yellow warning on cartridge holder

Supplies needed to give your injection:

- Humalog 200 units/ml KwikPen
- KwikPen compatible Needle (BD [Becton, Dickinson and Company] Pen Needles recommended)
- Swab

Needles and swab are not included.

Preparing your Pen

- Wash your hands with soap and water.
- Check the Pen to make sure you are taking the right type of insulin. This is especially important if you use more than 1 type of insulin.
- **Do not** use your Pen past the expiration date printed on the Label or for more than 28 days after you first start using the Pen.
- Always use a **new Needle** for each injection to help prevent infections and blocked Needles.

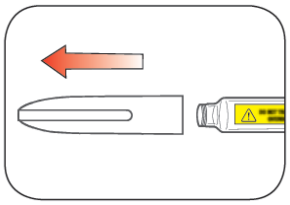
Step 1:

Pull the Pen Cap straight off.

- **Do not** remove the Pen Label.

Wipe the Rubber Seal with a swab.

Humalog 200 units/ml solution for injection should look clear and colourless. **Do not** use if it is cloudy, coloured, or has particles or clumps in it.

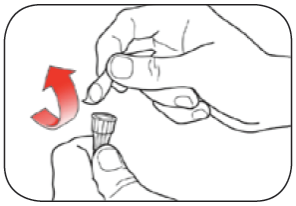




Step 2:

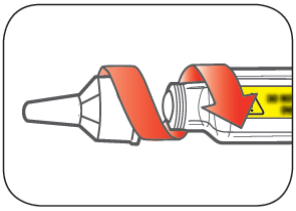
Select a new Needle.

Pull off the Paper Tab from the Outer Needle Shield.



Step 3:

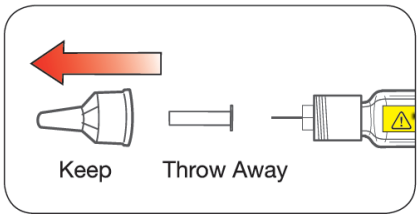
Push the capped Needle straight onto the Pen and twist the Needle on until it is tight.



Step 4:

Pull off the Outer Needle Shield. **Do not** throw it away.

Pull off the Inner Needle Shield and throw it away.



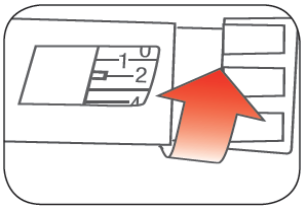
Priming your Pen

Prime before each injection.

- Priming your Pen means removing the air from the Needle and Cartridge that may collect during normal use and ensures that the Pen is working correctly.
- If you do not prime before each injection, you may get too much or too little insulin.

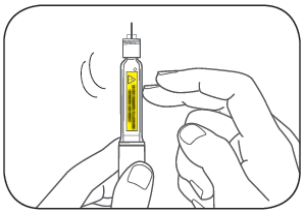
Step 5:

To prime your Pen, turn the Dose Knob to **select 2 units**.



Step 6:

Hold your Pen with the Needle pointing up. Tap the Cartridge Holder gently to collect air bubbles at the top.

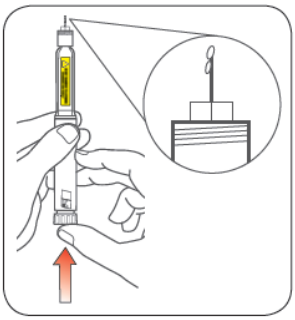


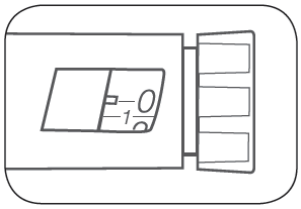
Step 7:

Continue holding your Pen with Needle pointing up. Push the Dose Knob in until it stops, and "**0**" is seen in the Dose Window. Hold the Dose Knob in and **count to 5 slowly**.

- You should see insulin at the tip of the Needle.
  - If you **do not** see insulin, repeat the priming steps, but not more than 8 times.
  - If you **still do not** see insulin, change the Needle and repeat the priming steps.

Small air bubbles are normal and will not affect your dose.





Selecting your dose

This pen has been designed to deliver the dose that is shown in the window. Dial your usual dose as instructed by your healthcare professional.

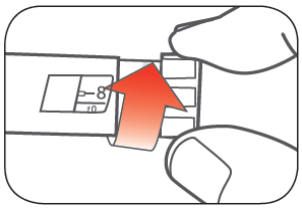
- You can give from 1 to 60 units in a single injection.
- If your dose is more than 60 units, you will need to give more than one injection.
  - If you need help deciding how to divide up your dose, ask your healthcare professional.
  - You should use a new Needle for each injection and repeat the priming step.

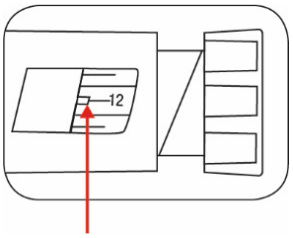
Step 8:

Turn the Dose Knob to select the number of units you need to inject. The Dose Indicator should line up with your dose.

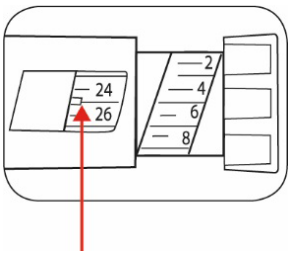
- The Pen dials 1 unit at a time.
- The Dose Knob clicks as you turn it.
- DO NOT dial your dose by counting the clicks because you may dial the wrong dose.
- The dose can be corrected by turning the Dose Knob in either direction until the correct dose lines up with the Dose Indicator.
- The **even** numbers are printed on the dial.
- The **odd** numbers, after the number 1, are shown as full lines.

Always check the number in the Dose Window to make sure you have dialled the correct dose.





(Example: 12 units shown in the Dose Window)



(Example: 25 units shown in the Dose Window)

- The Pen will not let you dial more than the number of units left in the Pen.
- If you need to inject more than the number of units left in the Pen, you may either:
  - inject the amount left in your Pen and then use a new Pen to give the rest of your dose, **or**
  - get a new Pen and inject the full dose.

Giving your injection

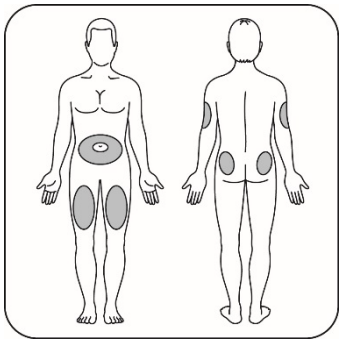
- Inject your insulin as your healthcare professional has shown you.
- Change (rotate) your injection site for each injection.
- **Do not** try to change your dose while injecting.

Step 9:

Choose your injection site.

Humalog 200 units/ml solution for injection is injected under the skin (subcutaneously) of your stomach area, buttocks, upper legs or upper arms.

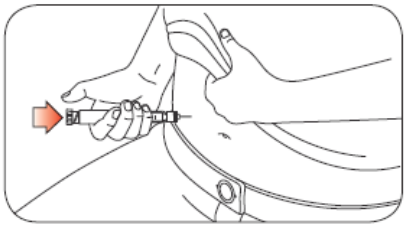
Wipe your skin with a swab, and let your skin dry before you inject your dose.



Step 10:

Insert the Needle into your skin.

Push the Dose Knob all the way in.



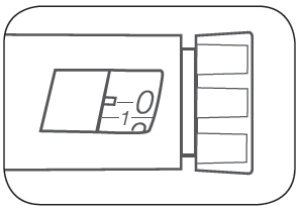


Continue to hold the Dose Knob in and **slowly count to 5** before removing the Needle.

Do not try to inject your insulin by turning the Dose Knob. You will NOT receive your insulin by turning the Dose Knob.

Step 11:

Pull the Needle out of your skin.



- A drop of insulin at the Needle tip is normal. It will not affect your dose.
- Check the number in the Dose Window.If you see “0” in the Dose Window, you have received the full amount you dialled.
- If you do not see “0” in the Dose Window, do not redial. Insert the needle into your skin and finish your injection.
- If you **still** do not think you received the full amount you dialled for your injection, **do not start over or repeat that injection**. Monitor your blood glucose as instructed by your healthcare professional.

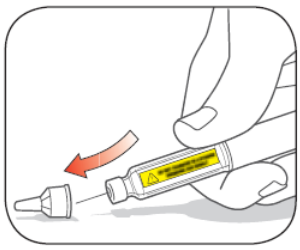
The plunger only moves a little with each injection and you may not notice that it moves.

If you see blood after you take the Needle out of your skin, press the injection site lightly with a piece of gauze or a swab. **Do not** rub the area.

After your injection

Step 12:

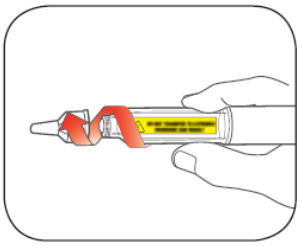
Carefully replace the Outer Needle Shield.



Step 13:

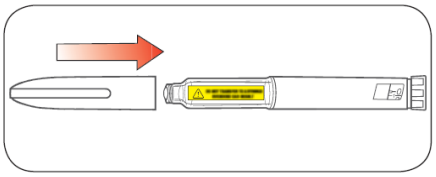
Unscrew the capped Needle and dispose of it as described below (see **Disposing of Pens and Needles** section).

Do not store the Pen with the Needle attached to prevent leaking, blocking the Needle, and air from entering the Pen.



Step 14:

Replace the Pen Cap by lining up the Cap Clip with the Dose Indicator and pushing straight on.



Disposing of Pens and Needles

- Put used Needles in a sharps container or hard plastic container with a secure lid. Do not throw needles directly into your household waste.
- Do not recycle the filled sharps container.
- Ask your healthcare professional about options to dispose of the Pen and the sharps container properly.
- The directions regarding needle handling are not intended to replace local, healthcare professional or institutional policies.

Storing your Pen

Unused Pens

- Store unused Pens in the refrigerator at 2°C to 8°C.
- **Do not** freeze Humalog 200 units/ml solution for injection. **Do not** use if it has been frozen.
- Unused Pens may be used until the expiration date printed on the Label, if the Pen has been kept in the refrigerator.

In-use Pen

- Store the Pen you are currently using at room temperature (below 30°C) and away from dust, food and liquids, heat and light.
- Throw away the Pen you are using after 28 days, even if it still has insulin left in it.

General information about the safe and effective use of your Pen

- **Keep your Pen and Needles out of the sight and reach of children.**
- **Do not** use your Pen if any part looks broken or damaged.
- Always carry an extra Pen in case yours is lost or damaged.

Troubleshooting

- If you cannot remove the Pen Cap, gently twist the cap back and forth, and then pull the cap straight off.
- If the Dose Knob is hard to push;
  - Pushing the Dose Knob more slowly will make it easier to inject.
  - Your Needle may be blocked. Put on a new Needle and prime the Pen.
  - You may have dust, food, or liquid inside the Pen. Throw the Pen away and get a new Pen. You may need to get a prescription from your healthcare professional.
- **Do not transfer insulin from the Pen to a syringe or an insulin pump. Severe overdose can result.**

If you have any questions or problems with your Humalog 200 units/ml KwikPen, call your healthcare professional for help or contact your local Lilly affiliate.

Document revision date:

Package leaflet: Information for the user

Humalog 100 units/ml Junior KwikPen solution for injection in a pre-filled pen
insulin lispro
Each Junior KwikPen delivers 0.5 – 30 units in steps of 0.5 units.

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Humalog Junior KwikPen is and what it is used for
2. What you need to know before you use Humalog Junior KwikPen
3. How to use Humalog Junior KwikPen
4. Possible side effects
5. How to store Humalog Junior KwikPen
6. Contents of the pack and other information

1. What Humalog Junior KwikPen is and what it is used for

Humalog Junior KwikPen is used to treat diabetes. Humalog works more quickly than normal human insulin because insulin lispro has been changed slightly in comparison to human insulin. Insulin lispro is closely related to human insulin which is a natural hormone made by the pancreas.

You get diabetes if your pancreas does not make enough insulin to control the level of glucose in your blood. Humalog is a substitute for your own insulin and is used to control glucose in the long term. It works very quickly and lasts a shorter time than soluble insulin (2 to 5 hours). You should normally use Humalog within 15 minutes of a meal.

Your doctor may tell you to use Humalog as well as a longer-acting insulin. Each kind of insulin comes with another patient information leaflet to tell you about it. Do not change your insulin unless your doctor tells you to.

Humalog is suitable for use in adults and children.

Humalog 100 units/ml Junior KwikPen is a disposable pre-filled pen containing 3 ml (300 units, 100 units/ml) of insulin lispro. One KwikPen contains multiple doses of insulin. The KwikPen dials half unit (0.5 unit) at a time. **The number of units are displayed in the dose window, always check this before your injection.** You can give from 0.5 unit to 30 units in a single injection. **If your dose is more than 30 units, you will need to give yourself more than one injection.**

2. What you need to know before you use Humalog Junior KwikPen

Do NOT use Humalog Junior KwikPen
- if you are **allergic** to insulin lispro or any of the other ingredients of this medicine (listed in section 6).
- if you think **hypoglycaemia** (low blood sugar) is starting. Further in this leaflet it tells you how to deal with mild hypoglycaemia (see Section 3: If you use more Humalog than you should).

Warnings and precautions

- Always check the pack and the label of the pre-filled pen for the name and type of the insulin when you get it from your pharmacy. Make sure you get the Humalog 100 units/ml Junior KwikPen that your doctor has told you to use.
- **Do NOT mix the Humalog 100 units/ml solution for injection in your pre-filled pen (the Junior KwikPen) with any other insulins or any other medicine**.
- If your blood sugar levels are well controlled by your current insulin therapy, you may not feel the warning symptoms when your blood sugar is falling too low. Warning signs are listed in section 4 of this leaflet. You must think carefully about when to have your meals, how often to exercise and how much to do. You must also keep a close watch on your blood sugar levels by testing your blood glucose often.
- A few people who have had hypoglycaemia after switching from animal insulin to human insulin have reported that the early warning symptoms were less obvious or different. If you often have hypoglycaemia or have difficulty recognising it, please discuss this with your doctor.
- If you answer YES to any of the following questions, tell your doctor, pharmacist or diabetes nurse
  - Have you recently become ill?
  - Do you have trouble with your kidneys or liver?
  - Are you exercising more than usual?
- You should also tell your doctor, pharmacist or diabetes nurse if you are planning to go abroad. The time difference between countries may mean that you have to have your injections and meals at different times from when you are at home.
- Some patients with long-standing type 2 diabetes mellitus and heart disease or previous stroke who were treated with pioglitazone and insulin experienced the development of heart failure. Inform your doctor as soon as possible, if you experience signs of heart failure such as unusual shortness of breath or rapid increase in weight or localised swelling (oedema).
- This Pen is not recommended for use by the blind or visually impaired without the help of someone trained to use the Pen.

Skin changes at the injection site

The injection site should be rotated to prevent skin changes such as lumps under the skin. The insulin may not work very well if you inject into a lumpy area (See How to use Humalog Junior KwikPen). Contact your doctor if you are currently injecting into a lumpy area before you start injecting a different area. Your doctor may tell you to check your blood sugar more closely, and to adjust your insulin or your other antidiabetic medications dose.

Other medicines and Humalog Junior KwikPen

Your insulin needs may change if you are taking

- the contraceptive pill,
- steroids,
- thyroid hormone replacement therapy,
- oral hypoglycaemics, (e.g. metformin, acarbose, sulphonylurea agents, pioglitazone, empagliflozin, DPP-4-inhibitors like sitagliptin or saxagliptine,),
- acetyl salicylic acid,
- sulpha antibiotics,
- somatostatin analogues (such as octreotide, used to treat an uncommon condition in which you make too much growth hormone),
- "beta$_2$ stimulants"such as salbutamol or terbutaline to treat asthma, or ritodrine used to stop premature labor,
- beta-blockers – to treat high blood pressure., or
- some antidepressants (monoamine oxidase inhibitors or selective serotonin reuptake inhibitors),
- danazol (medicine acting on ovulation),
- some angiotensin converting (ACE) inhibitors, used to treat certain heart conditions or high blood pressure (for example captopril, enalapril), and
- specific medicines to treat high blood pressure, kidney damage due to diabetes, and some heart problems (angiotensin II receptor blockers).

Please tell your doctor, if you are taking, have recently taken or might take any other medicines. (see also section “Warnings and precautions”).

Humalog with alcohol
Your blood sugar levels may either rise or fall if you drink alcohol. Therefore the amount of insulin needed may change.

Pregnancy and breast-feeding
Are you pregnant or thinking about becoming pregnant, or are you breast-feeding? The amount of insulin you need usually falls during the first three months of pregnancy and increases for the remaining six months. If you are breast-feeding, you may need to alter your insulin intake or diet. Ask your doctor for advice.

Driving and using machines
Your ability to concentrate and react may be reduced if you have hypoglycaemia. Please keep this possible problem in mind in all situations where you might put yourself and others at risk (e.g. driving a car or operating machinery). You should contact your doctor about the advisability of driving if you have:
- frequent episodes of hypoglycaemia
- reduced or absent warning signs of hypoglycaemia

Humalog Junior KwikPen contains sodium
This medicine contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially ‘sodium-free’.

3. How to use Humalog Junior KwikPen

Always use this medicine exactly as your doctor has told you. You should check with your doctor if you are not sure. To prevent the possible transmission of disease, each pen must be used by you only, even if the needle is changed.

Dose
- The number of half units (0.5 units) is shown in the dose window of your pen. The half units (0.5 units) are shown as lines between the numbers.
- Always check the number in the dose window to make sure you have dialled the correct dose.
- You should normally inject Humalog within 15 minutes of a meal. If you need to, you can inject soon after a meal. But your doctor will have told you exactly how much to use, when to use it, and how often. These instructions are only for you. Follow them exactly and visit your diabetes clinic regularly.
- If you change the type of insulin you use (for example from a human or animal insulin to a Humalog product), you may have to take more or less than before. This might just be for the first injection or it may be a gradual change over several weeks or months.
- Humalog KwikPen is only suitable for injecting just under the skin. Speak to your doctor if you need to inject your insulin by another method.

Preparing Humalog Junior KwikPen
- Humalog is already dissolved in water, so you do not need to mix it. But you must use it **only** if it looks like water. It must be clear, have no colour and no solid pieces in it. Check each time you inject yourself.

Getting the Junior KwikPen ready to use (Please see user manual)
- First wash your hands.
- Read the instructions on how to use your pre-filled insulin pen. Please follow the instructions carefully. Here are some reminders.
- Use a clean needle. (Needles are not included).

- Prime your Junior KwikPen before each use. This checks that insulin comes out and clears the air bubbles from your Junior KwikPen . There may still be some small air bubbles left in the pen - these are harmless. But if the air bubbles are too large it may affect the insulin dose.

Injecting Humalog
- Before you make an injection, clean your skin as you have been instructed. Inject under the skin, as you were taught. Do not inject directly into a vein. After your injection, leave the needle in the skin for five seconds to make sure you have taken the whole dose. Do not rub the area you have just injected. Make sure you inject at least half an inch (1 cm) from the last injection and that you 'rotate' the places you inject, as you have been taught. It doesn't matter which injection site you use, either upper arm, thigh, buttock or abdomen, your Humalog injection will still work quicker than soluble human insulin.
- You must not administer Humalog by the intravenous route. Inject Humalog as your physician or nurse has taught you. Only your physician can administer Humalog by the intravenous route. He will only do this under special circumstances such as surgery or if you are ill and your glucose levels are too high.

After injecting
- As soon as you have done the injection, unscrew the needle from the Junior KwikPen using the outer needle cap. This will keep the insulin sterile and stop it leaking. It also stops air entering the pen and your needle clogging. **Do not share your needles**. Do not share your pen. Replace the cap on your pen.

Further injections
- Every time you use a Junior KwikPen you must use a new needle. Before every injection, clear any air bubbles. You can see how much insulin is left by holding the Junior KwikPen with the needle pointing up. The scale on the cartridge shows about how many units you have left.
- Once the Junior KwikPen is empty, do not use it again. Please get rid of it carefully - your pharmacist or diabetes nurse will tell you how to do this.

Using Humalog in an infusion pump
- Junior KwikPen is only suitable for injecting just under the skin. Do not use the pen to administer Humalog by a different way. Other forms of Humalog 100 units/ml are available if this is necessary. Speak to your doctor if this applies to you.

If you use more Humalog than you should
If you use more Humalog than you need or are unsure how much you have injected, a low blood sugar may occur. Check your blood sugar.

If your blood sugar is low **(mild hypoglycaemia)**, eat glucose tablets, sugar or drink a sugary drink. Then eat fruit, biscuits, or a sandwich, as your doctor has advised you and have some rest. This will often get you over mild hypoglycaemia or a minor insulin overdose. If you get worse and your breathing is shallow and your skin gets pale, tell your doctor at once. A glucagon injection can treat quite severe hypoglycaemia. Eat glucose or sugar after the glucagon injection. If you do not respond to glucagon, you will have to go to hospital. Ask your doctor to tell you about glucagon.

If you forget to use Humalog
If you take less Humalog than you need or are unsure how much you have injected, a high blood sugar may occur. Check your blood sugar

If hypoglycaemia (low blood sugar) or hyperglycaemia (high blood sugar) is not treated they can be very serious and cause headaches, feeling sick (nausea), being sick (vomiting), loss of fluids (dehydration), unconsciousness, coma or even death (see section 4 "Possible Side Effects").

Three simple steps to avoid hypoglycaemia or hyperglycaemia are:
- Always carry a spare pen in case you lose your Junior KwikPen or it gets damaged.
- Always carry something to show you are diabetic.

- Always carry sugar with you.

If you stop using Humalog.
If you take less Humalog than you need, a high blood sugar may occur. Do not change your insulin unless your doctor tells you to.

If you have any further questions on the use of this product, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Severe allergy is rare (may affect up to 1 in 1,000 people). The symptoms are as follows:
- rash over the whole body
- difficulty in breathing
- wheezing
- blood pressure dropping
- heart beating fast
- sweating

If you think you are having this sort of insulin allergy with Humalog, contact a doctor at once.

Local allergy is common (may affect up to 1 in 10 people). Some people get redness, swelling or itching around the area of the insulin injection. This usually clears up in anything from a few days to a few weeks. If this happens to you, tell your doctor.

Lipodystrophy is uncommon (may affect up to 1 in 100 people). If you inject insulin too often at the same place, the fatty tissue may either shrink (lipoatrophy) or thicken (lipohypertrophy). Lumps under the skin may also be caused by build-up of a protein called amyloid (cutaneous amyloidosis). The insulin may not work very well if you inject into a lumpy area. Change the injection site with each injection to help prevent these skin changes.

Oedema (e.g. swelling in arms, ankles; fluid retention) has been reported, particularly at the start of insulin therapy or during a change in therapy to improve control of your blood glucose.

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

Common problems of diabetes

Hypoglycaemia
Hypoglycaemia (low blood sugar) means there is not enough sugar in the blood. This can be caused if:
- you take too much Humalog or other insulin;
- you miss or delay meals or change your diet;
- you exercise or work too hard just before or after a meal;
- you have an infection or illness (especially diarrhoea or vomiting);
- there is a change in your need for insulin; or
- you have trouble with your kidneys or liver which gets worse.

Alcohol and some medicines can affect your blood sugar levels (see section 2).

The first symptoms of low blood sugar usually come on quickly and include the following:
- tiredness
- nervousness or shakiness
- headache
- rapid heartbeat
- feeling sick
- cold sweat

While you are not confident about recognising your warning symptoms, avoid situations such as driving a car, in which you or others would be put at risk by hypoglycaemia.

Hyperglycaemia and diabetic ketoacidosis
Hyperglycaemia (too much sugar in the blood) means that your body does not have enough insulin. Hyperglycaemia can be brought about by:
- not taking your Humalog or other insulin;
- taking less insulin than your doctor tells you to;
- eating a lot more than your diet allows; or
- fever, infection or emotional stress.

Hyperglycaemia can lead to diabetic ketoacidosis. The first symptoms come on slowly over many hours or days. The symptoms include the following:
- feeling sleepy
- flushed face
- thirst
- no appetite
- fruity smell on the breath
- feeling or being sick

Severe symptoms are heavy breathing and a rapid pulse. **Get medical help immediately.**

Illness
If you are ill, especially if you feel sick or are sick, the amount of insulin you need may change. **Even when you are not eating normally, you still need insulin.** Test your urine or blood, follow your 'sick rules', and tell your doctor.

5. How to store Humalog Junior KwikPen

Keep out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the label and the carton. The expiry date refers to the last day of that month.

Before the first use store your Humalog Junior KwikPen in a refrigerator (2°C – 8°C). Do not freeze.

Keep your Humalog Junior KwikPen in use at room temperature (below 30°C) and discard after 28 days **even if some of the solution remains**. Do not put it near heat or in the sun. Do not keep the Junior KwikPen that you are using in the fridge. The Junior KwikPen should not be stored with the needle attached.

Do not use this medicine if you notice the solution is coloured or it has solid pieces in it. You must use it **only** if it looks like water. Check this each time you inject yourself.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. Contents of the pack and other information

What Humalog 100 units/ml Junior KwikPen solution for injection contains
- The active substance is insulin lispro. Each ml of solution contains 100 units (U) of insulin lispro. Each pre-filled pen (3 ml) contains 300 units (U) of insulin lispro.
- The other ingredients are metacresol, glycerol, dibasic sodium phosphate 7 H_2O, zinc oxide and water for injections. Sodium hydroxide or hydrochloric acid may have been used to adjust the acidity.

What Humalog 100 units/ml Junior KwikPen looks like and contents of the pack
Humalog 100 units/ml Junior KwikPen solution for injection is a sterile, clear, colourless, aqueous solution and contains 100 units of insulin lispro in each millilitre (100 units/ml) solution for injection. Each Humalog Junior KwikPen contains 300 units (3 millilitres). The Humalog Junior KwikPen comes in a pack of 1or 5 pre-filled pens or multipacks of 2 x 5 pre-filled pens. Not all pack sizes may be marketed. The Junior KwikPen simply has a built in cartridge. When the pre-filled pen is empty you cannot use it again. The Junior KwikPen is blue. The dose knob is blue with raised ridges. The label is white with an orange colour bar and there is an orange to yellow, burgundy colour band. Each Junior KwikPen delivers 0.5 – 30 units in steps of 0.5 units.

Marketing Authorisation Holder

Eli Lilly Nederland B.V., Orteliuslaan 1000, 3528 BD Utrecht, The Netherlands.

Manufacturer

Lilly France S.A.S., Rue du Colonel Lilly, 67640 Fegersheim, France,

For any information about this medicinal product, please contact the local representative of the Marketing Authorisation Holder:

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This leaflet was last revised in {MM/YYYY}.

USER MANUAL

Please see manual text later.

Detailed information on this medicine is available on the European Medicines Agency web site: https://www.ema.europa.eu.

Instructions for Use

Humalog 100 units/ml Junior KwikPen solution for injection in a pre-filled pen
insulin lispro



PLEASE READ THESE INSTRUCTIONS BEFORE USE

Read the Instructions for Use before you start taking Humalog Junior KwikPen and each time you get another Humalog Junior KwikPen. There may be new information. This information does not take the place of talking to your healthcare professional about your medical condition or your treatment.

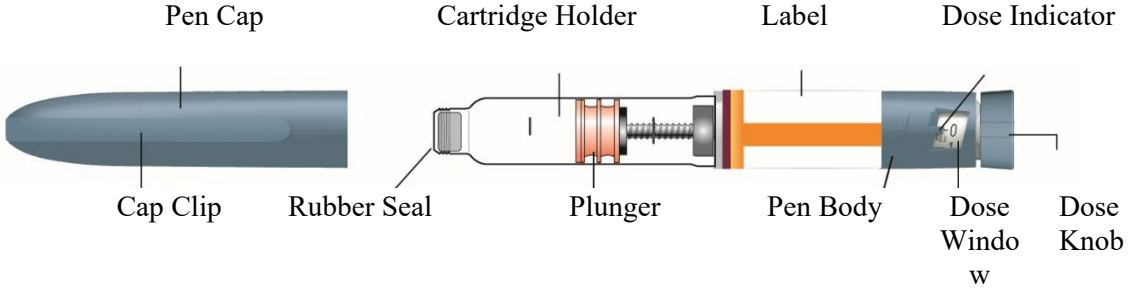
Humalog 100 units/ml Junior KwikPen ("Pen") is a disposable pre-filled pen containing 3 ml (300 units, 100 units/ml) of insulin lispro solution for injection. One pen contains multiple doses of insulin.

- Your healthcare professional will tell you how many units to give as your dose and how to inject your prescribed dose of insulin.
- The Pen dials half unit (0.5 unit) at a time. You can give from 0.5 unit to 30 units in a single injection.
- Always check the number in the dose window to make sure you have dialed the correct dose.
- If your dose is more than 30 units, you will need to give yourself more than one injection.
- The Plunger only moves a little with each injection, and you may not notice that it moves. When the Plunger reaches the end of the cartridge, you have used all 300 units in the Pen.

Do not share your Pen with other people, even if the needle has been changed. Do not reuse or share needles with other people. You may give an infection to them or get an infection from them.

This Pen is not recommended for use by the blind or visually impaired without the help of someone trained to use the Pen.

Humalog Junior KwikPen Parts

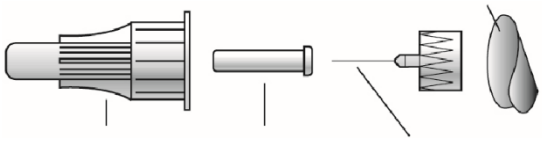


Pen Needle Parts
(Needles Not Included)

Dose Knob

Blue, with raised ridges on end and side

Paper Tab





How to recognize your Humalog Junior KwikPen:

- Pen colour: Blue
- Dose Knob: Blue, with raised ridges on end and side
- Label: White with an orange colour bar and orange-to-yellow and burgundy colour band

Supplies needed to give your injection:

- Humalog Junior KwikPen
- KwikPen compatible Needle (BD [Becton, Dickinson and Company] Pen Needles recommended)
- Swab

Needles and swab are not included.

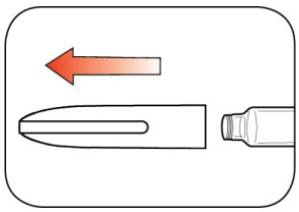
Preparing your Pen

- Wash your hands with soap and water.
- Check the Pen to make sure you are taking the right type of insulin. This is especially important if you use more than 1 type of insulin.
- **Do not** use your Pen past the expiration date printed on the Label or for more than 28 days after you first start using the Pen.
- Always use a **new Needle** for each injection to help prevent infections and blocked Needles.

Step 1:

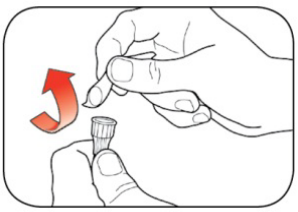
- Pull the Pen Cap straight off.
  - **Do not** remove the Pen Label.
- Wipe the Rubber Seal with a swab.

Humalog should look clear and colourless. **Do not** use if it is cloudy, coloured, or has particles or clumps in it.



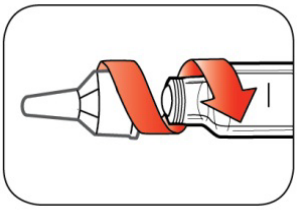
Step 2:

- Select a new Needle.
- Pull off the Paper Tab from the Outer Needle Shield.



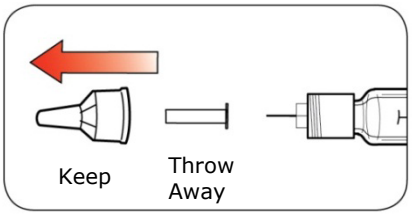
Step 3:

- Push the capped Needle straight onto the Pen and twist the Needle on until it is tight.



Step 4:

- Pull off the Outer Needle Shield. **Do not** throw it away.
- Pull off the Inner Needle Shield and throw it away.



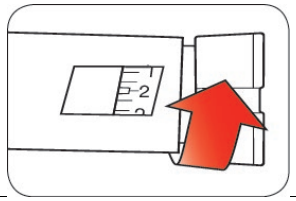
Priming your Pen

Prime before each injection.

- Priming your Pen means removing the air from the Needle and Cartridge that may collect during normal use. It is important to prime your Pen so that it will work correctly.
- If you **do not** prime before each injection, you may get too much or too little insulin.

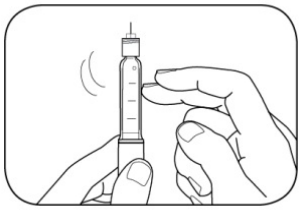
Step 5:

- To prime your Pen, turn the Dose Knob to select 2 units.



Step 6:

- Hold your Pen with the Needle pointing up. Tap the Cartridge Holder gently to collect air bubbles at the top.



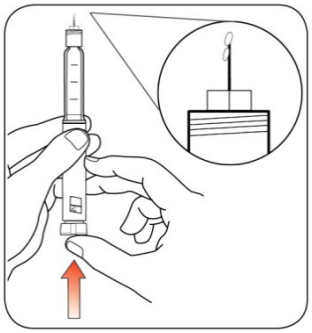
Step 7:

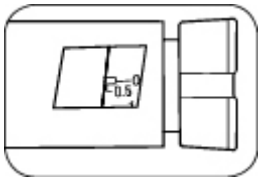
- Continue holding your Pen with the Needle pointing up. Push the Dose Knob in until it stops, and "**0**" is seen in the Dose Window. Hold the Dose Knob in and **count to 5 slowly**.

You should see insulin at the tip of the Needle.

  - If you **do not** see insulin, repeat the priming steps, but not more than 4 times.
  - If you **still do not** see insulin, change the Needle and repeat the priming steps.

Small air bubbles are normal and will not affect your dose.





Selecting your dose

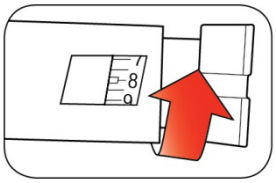
- You can give from half unit (0.5 unit) to 30 units in a single injection.

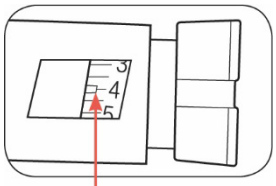
Always check the number in the Dose Window to make sure you have dialled the correct dose.

- If your dose is more than 30 units, you will need to give more than one injection.
  - Talk to your healthcare professional about how to give your dose.
  - Use a new Needle for each injection and repeat the priming step.
  - If you **usually** need more than 30 units, ask your healthcare professional if a different Humalog KwikPen would be better for you.

Step 8:

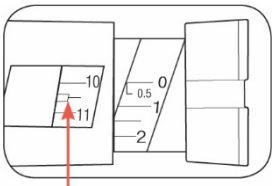
- Turn the Dose Knob to select the number of units you need to inject. The Dose Indicator should line up with your dose.
  - The Pen dials half unit (0.5 unit) at a time.
  - The Dose Knob clicks as you turn it.
  - **DO NOT** dial your dose by counting the clicks because you may dial the wrong dose.
  - The dose can be corrected by turning the Dose Knob in either direction until the correct dose lines up with the Dose Indicator.
  - The **whole unit** numbers are printed on the dial.





Example: 4 units shown in the Dose Window

  - The **half units** are shown as lines between the numbers.



Example: 10 ½ (10.5) units shown in the Dose Window

- **Always check the number in the Dose Window to make sure you have dialled the correct dose.**

- The Pen will not let you dial more than the number of units left in the Pen.
- If you need to inject more than the number of units left in the Pen, you may either:
  - inject the amount left in your Pen and then use a new Pen to give the rest of your dose, **or**
  - get a new Pen and inject the full dose.
- It is normal to see a small amount of insulin left in the Pen that you can not inject.

Giving your injection

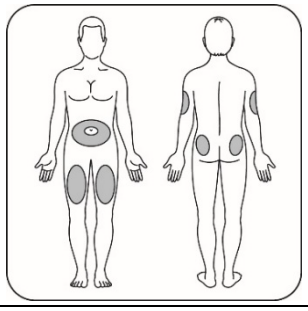
- Inject your insulin as your healthcare professional has shown you.
- Change (rotate) your injection site for each injection.
- **Do not** try to change your dose while injecting.

Step 9:

- Choose your injection site.

  Humalog is injected under the skin (subcutaneously) of your stomach area, buttocks, upper legs or upper arms.

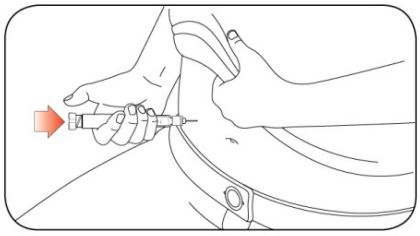
- Wipe your skin with a swab, and let your skin dry before you inject your dose.



Step 10:

- Insert the Needle into your skin.
- Push the Dose Knob all the way in.
- Continue to hold the Dose Knob in and **slowly count to 5** before removing the Needle.

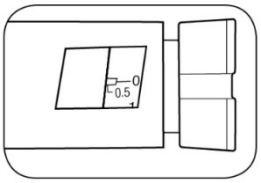




Do not try to inject your insulin by turning the Dose Knob. You will **NOT** receive your insulin by turning the Dose Knob.

Step 11:

- Pull the Needle out of your skin.
  - A drop of insulin at the Needle tip is normal. It will not affect your dose.
- Check the number in the Dose Window
  - If you see “0” in the Dose window, you have received the full amount you dialled.
  - If you do not see “0” in the Dose window, you did not receive your full dose. **Do not** redial. Insert the needle into your skin and finish your injection.
  - If you **still** do not think you received the full amount you dialled for your injection, **do not start over or repeat that injection**. Monitor your blood glucose and call your healthcare professional for further instructions.



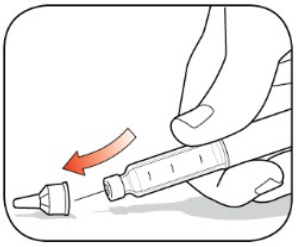
The plunger only moves a little with each injection, and you may not notice that it moves.

If you see blood after you take the Needle out of your skin, press the injection site lightly with a piece of gauze or a swab. **Do not** rub the area.

After your injection

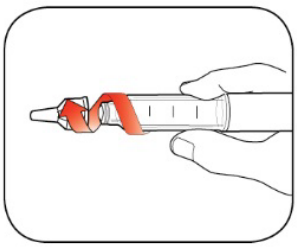
Step 12:

- Carefully replace the Outer Needle Shield.



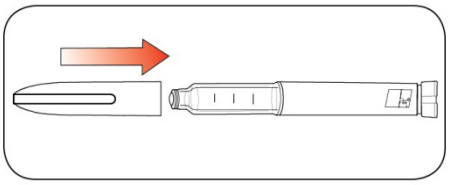
Step 13:

- Unscrew the capped Needle and dispose of it as described below (see **Disposing of Pens and Needles** section).
- Do not store the Pen with the Needle attached to prevent leaking, blocking the Needle, and air from entering the Pen.



Step 14:

- Replace the Pen Cap by lining up the Cap Clip with the Dose Indicator and pushing straight on.



Disposing of Pens and Needles

- Put used Needles in a sharps container or a hard plastic container with a secure lid. **Do not** throw needles directly into your household waste.
- **Do not** recycle the filled sharps container.
- Ask your healthcare professional about options to dispose of the Pen and the sharps container properly.
- The directions regarding needle handling are not intended to replace local, healthcare professional or institutional policies.

Storing your Pen

Unused Pens

- Store unused Pens in the refrigerator at (2 °C to 8 °C).
- **Do not** freeze Humalog. **Do not** use if it has been frozen.
- Unused Pens may be used until the expiration date printed on the Label, if the Pen has been kept in the refrigerator.

In-use Pen

- Store the Pen you are currently using at room temperature (below 30 °C) and away from dust, food and liquids, heat and light.
- Throw away the Pen you are using after 28 days, even if it still has insulin left in it.

General information about the safe and effective use of your Pen

- **Keep your Pen and Needles out of the sight and reach of children.**
- **Do not** use your Pen if any part looks broken or damaged.
- Always carry an extra Pen in case yours is lost or damaged.

Troubleshooting

- If you can not remove the Pen Cap, gently twist the cap back and forth, and then pull the cap straight off.
- If the Dose Knob is hard to push:
  - Pushing the Dose Knob more slowly will make it easier to inject.
  - Your Needle may be blocked. Put on a new Needle and prime the Pen.
  - You may have dust, food, or liquid inside the Pen. Throw the Pen away and get a new Pen. You may need to get a prescription from your healthcare professional.

If you have any questions or problems with your Humalog 100 units/ml Junior KwikPen, call your healthcare professional for help or contact your local Lilly affiliate.

Document revision date:

Package leaflet: Information for the user

Humalog 100 units/ml Tempo Pen solution for injection in a pre-filled pen
insulin lispro
Each Tempo Pen delivers 1 – 60 units in steps of 1 units.

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Humalog Tempo Pen is and what it is used for
2. What you need to know before you use Humalog Tempo Pen
3. How to use Humalog Tempo Pen
4. Possible side effects
5. How to store Humalog Tempo Pen
6. Contents of the pack and other information

1. What Humalog Tempo Pen is and what it is used for

Humalog Tempo Pen is used to treat diabetes. Humalog works more quickly than normal human insulin because the insulin molecule has been changed slightly in comparison to human insulin. Insulin lispro is closely related to human insulin which is a natural hormone made by the pancreas.

You get diabetes if your pancreas does not make enough insulin to control the level of glucose in your blood. Humalog is a substitute for your own insulin and is used to control glucose in the long term. It works very quickly and lasts a shorter time than soluble insulin (2 to 5 hours). You should normally use Humalog within 15 minutes of a meal.

Your doctor may tell you to use Humalog Tempo Pen as well as a longer-acting insulin. Each kind of insulin comes with another patient information leaflet to tell you about it. Do not change your insulin unless your doctor tells you to.

Humalog is suitable for use in adults and children.

The Tempo Pen is a disposable pre-filled pen containing 3 ml (300 units, 100 units/ml) of insulin lispro. One Tempo Pen contains multiple doses of insulin. The Tempo Pen dials 1 unit at a time. **The number of units are displayed in the dose window, always check this before your injection.** You can give from 1 to 60 units in a single injection. **If your dose is more than 60 units, you will need to give yourself more than one injection.**

2. What you need to know before you use Humalog Tempo Pen

Do NOT use Humalog Tempo Pen
- if you think **hypoglycaemia** (low blood sugar) is starting. Further in this leaflet it tells you how to deal with mild hypoglycaemia (see Section 3: If you use more Humalog than you should).
- if you are **allergic** to insulin lispro or any of the other ingredients of this medicine (listed in section 6).

Warnings and precautions

- Always check the pack and the label of the pre-filled pen for the name and type of the insulin when you get it from your pharmacy. Make sure you get the Humalog 100 units/ml Tempo Pen that your doctor has told you to use.
- If your blood sugar levels are well controlled by your current insulin therapy, you may not feel the warning symptoms when your blood sugar is falling too low. Warning signs are listed in section 4 of this leaflet. You must think carefully about when to have your meals, how often to exercise and how much to do. You must also keep a close watch on your blood sugar levels by testing your blood glucose often.
- A few people who have had hypoglycaemia after switching from animal insulin to human insulin have reported that the early warning symptoms were less obvious or different. If you often have hypoglycaemia or have difficulty recognising it, please discuss this with your doctor.
- If you answer YES to any of the following questions, tell your doctor, pharmacist or diabetes nurse
  - Have you recently become ill?
  - Do you have trouble with your kidneys or liver?
  - Are you exercising more than usual?
- The amount of insulin you need may also change if you drink alcohol.
- You should also tell your doctor, pharmacist or diabetes nurse if you are planning to go abroad. The time difference between countries may mean that you have to have your injections and meals at different times from when you are at home.
- Some patients with long-standing type 2 diabetes mellitus and heart disease or previous stroke who were treated with pioglitazone and insulin experienced the development of heart failure. Inform your doctor as soon as possible, if you experience signs of heart failure such as unusual shortness of breath or rapid increase in weight or localised swelling (oedema).
- This Pen is not recommended for use by the blind or visually impaired without the help of someone trained to use the Pen.
- The Tempo Pen contains a magnet. If you have a medical device fitted, such as a heart pacemaker, this may not work correctly if the Tempo Pen is held too close. The magnetic field extends to approximately 1.5 cm.

Skin changes at the injection site

The injection site should be rotated to prevent skin changes such as lumps under the skin. The insulin may not work very well if you inject into a lumpy area (See How to use Humalog Tempo Pen). Contact your doctor if you are currently injecting into a lumpy area before you start injecting a different area. Your doctor may tell you to check your blood sugar more closely, and to adjust your insulin or your other antidiabetic medications dose.

Other medicines and Humalog Tempo Pen

Your insulin needs may change if you are taking

- the contraceptive pill,
- steroids,
- thyroid hormone replacement therapy,
- oral hypoglycaemics,
- acetyl salicylic acid,
- sulpha antibiotics,
- octreotide,
- "beta$_2$ stimulants" (for example ritodrine, salbutamol or terbutaline),
- beta-blockers, or
- some antidepressants (monoamine oxidase inhibitors or selective serotonin reuptake inhibitors),
- danazol,
- some angiotensin converting enzyme (ACE) inhibitors (for example captopril, enalapril), and
- angiotensin II receptor blockers.

Please tell your doctor, if you are taking, have recently taken or might take any other medicines, including medicines obtained without a prescription (see section "Warnings and precautions").

Humalog with alcohol
Your blood sugar levels may either rise or fall if you drink alcohol. Therefore the amount of insulin needed may change.

Pregnancy and breast-feeding
Are you pregnant or thinking about becoming pregnant, or are you breast-feeding? The amount of insulin you need usually falls during the first three months of pregnancy and increases for the remaining six months. If you are breast-feeding, you may need to alter your insulin intake or diet. Ask your doctor for advice.

Driving and using machines
Your ability to concentrate and react may be reduced if you have hypoglycaemia. Please keep this possible problem in mind in all situations where you might put yourself and others at risk (e.g. driving a car or operating machinery). You should contact your doctor about the advisability of driving if you have:
- frequent episodes of hypoglycaemia
- reduced or absent warning signs of hypoglycaemia

Humalog Tempo Pen contains sodium
This medicine contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially 'sodium-free'.

3. How to use Humalog Tempo Pen

Always use this medicine exactly as your doctor has told you. You should check with your doctor if you are not sure. To prevent the possible transmission of disease, each pen must be used by you only, even if the needle is changed.

Dose
- Always check the number in the dose window to make sure you have dialled the correct dose.
- You should normally inject Humalog within 15 minutes of a meal. If you need to, you can inject soon after a meal. But your doctor will have told you exactly how much to use, when to use it, and how often. These instructions are only for you. Follow them exactly and visit your diabetes clinic regularly.
- If you change the type of insulin you use (for example from a human or animal insulin to a Humalog product), you may have to take more or less than before. This might just be for the first injection or it may be a gradual change over several weeks or months.
- Humalog Tempo Pen is only suitable for injecting just under the skin. Speak to your doctor if you need to inject your insulin by another method.

Preparing Humalog Tempo Pen
- Humalog is already dissolved in water, so you do not need to mix it. But you must use it **only** if it looks like water. It must be clear, have no colour and no solid pieces in it. Check each time you inject yourself.

Getting the Tempo Pen ready to use (Please see user manual)
- First wash your hands.
- Read the instructions on how to use your pre-filled insulin pen. Please follow the instructions carefully. Here are some reminders.
- Use a clean needle. (Needles are not included).
- Prime your Tempo Pen before each use. This checks that insulin comes out and clears the air bubbles from your Tempo Pen. There may still be some small air bubbles left in the pen - these are harmless. But if the air bubbles are too large it may affect the insulin dose.

Injecting Humalog

- Before you make an injection, clean your skin as you have been instructed. Inject under the skin, as you were taught. Do not inject directly into a vein. After your injection, leave the needle in the skin for five seconds to make sure you have taken the whole dose. Do not rub the area you have just injected. Make sure you inject at least half an inch (1 cm) from the last injection and that you 'rotate' the places you inject, as you have been taught. It doesn't matter which injection site you use, either upper arm, thigh, buttock or abdomen, your Humalog injection will still work quicker than soluble human insulin.
- You must not administer Humalog by the intravenous route. Inject Humalog as your physician or nurse has taught you. Only your physician can administer Humalog by the intravenous route. He will only do this under special circumstances such as surgery or if you are ill and your glucose levels are too high.

After injecting

- As soon as you have done the injection, unscrew the needle from the Tempo Pen using the outer needle cap. This will keep the insulin sterile and stop it leaking. It also stops air entering the pen and your needle clogging. **Do not share your needles**. Do not share your pen. Replace the cap on your pen.

If you are unsure how much you have injected then check your blood sugar levels before deciding if you need another injection.

Further injections

- Every time you use a Tempo Pen you must use a new needle. Before every injection, clear any air bubbles. You can see how much insulin is left by holding the Tempo Pen with the needle pointing up. The scale on the cartridge shows about how many units you have left.
- Do NOT mix the Humalog 100 units/ml solution for injection in your pre-filled pen with any other insulins or any other medicine.
- Once the Tempo Pen is empty, do not use it again. Please get rid of it carefully - your pharmacist or diabetes nurse will tell you how to do this.

Tempo Smart Button

The Tempo Pen is designed to work with the Tempo Smart Button. The optional additional feature Tempo Smart Button is a product available for the Tempo Pen, which may be used for transmitting dose information to a mobile application. The Tempo Pen can be used with or without the Tempo Smart Button attached. See instructions provided with the Tempo Smart Button and the mobile application for further information.

Using Humalog in an infusion pump

- Tempo Pen is only suitable for injecting just under the skin. Do not use the pen to administer Humalog by a different way. Other forms of Humalog 100 units/ml are available if this is necessary. Speak to your doctor if this applies to you.

If you use more Humalog than you should

If you use more Humalog than you need or are unsure how much you have injected**,** a low blood sugar may occur. Check your blood sugar.

If your blood sugar is low **(mild hypoglycaemia)**, eat glucose tablets, sugar or drink a sugary drink. Then eat fruit, biscuits, or a sandwich, as your doctor has advised you and have some rest. This will often get you over mild hypoglycaemia or a minor insulin overdose. If you get worse and your breathing is shallow and your skin gets pale, tell your doctor at once. A glucagon injection can treat quite severe hypoglycaemia. Eat glucose or sugar after the glucagon injection. If you do not respond to glucagon, you will have to go to hospital. Ask your doctor to tell you about glucagon.

If you forget to use Humalog
If you take less Humalog than you need or are unsure how much you have injected, a high blood sugar may occur. Check your blood sugar

If hypoglycaemia (low blood sugar) or hyperglycaemia (high blood sugar) is not treated they can be very serious and cause headaches, feeling sick (nausea), being sick (vomiting), loss of fluids (dehydration), unconsciousness, coma or even death (see section 4 "Possible Side Effects").

Three simple steps to avoid hypoglycaemia or hyperglycaemia are:
- Always carry a spare pen in case you lose your Tempo Pen or it gets damaged.
- Always carry something to show you are diabetic.
- Always carry sugar with you.

If you stop using Humalog.
If you use less Humalog than you need, a high blood sugar may occur. Do not change your insulin unless your doctor tells you to.

If you have any further questions on the use of this product, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Severe allergy is rare (may affect up to 1 in 1,000 people). The symptoms are as follows:
- rash over the whole body
- difficulty in breathing
- wheezing
- blood pressure dropping
- heart beating fast
- sweating

If you think you are having this sort of insulin allergy with Humalog, contact a doctor at once.

Local allergy is common (may affect up to 1 in 10 people). Some people get redness, swelling or itching around the area of the insulin injection. This usually clears up in anything from a few days to a few weeks. If this happens to you, tell your doctor.

Lipodystrophy is uncommon (may affect up to 1 in 100 people). If you inject insulin too often at the same place, the fatty tissue may either shrink (lipoatrophy) or thicken (lipohypertrophy). Lumps under the skin may also be caused by build-up of a protein called amyloid (cutaneous amyloidosis). The insulin may not work very well if you inject into a lumpy area. Change the injection site with each injection to help prevent these skin changes.

Oedema (e.g. swelling in arms, ankles; fluid retention) has been reported, particularly at the start of insulin therapy or during a change in therapy to improve control of your blood glucose.

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

Common problems of diabetes

A. Hypoglycaemia
Hypoglycaemia (low blood sugar) means there is not enough sugar in the blood. This can be caused if:
- you take too much Humalog or other insulin;
- you miss or delay meals or change your diet;
- you exercise or work too hard just before or after a meal;

- you have an infection or illness (especially diarrhoea or vomiting);
- there is a change in your need for insulin; or
- you have trouble with your kidneys or liver which gets worse.

Alcohol and some medicines can affect your blood sugar levels (see section 2).

The first symptoms of low blood sugar usually come on quickly and include the following:
- tiredness
- nervousness or shakiness
- headache
- rapid heartbeat
- feeling sick
- cold sweat

While you are not confident about recognising your warning symptoms, avoid situations, e.g. driving a car, in which you or others would be put at risk by hypoglycaemia.

B. Hyperglycaemia and diabetic ketoacidosis
Hyperglycaemia (too much sugar in the blood) means that your body does not have enough insulin. Hyperglycaemia can be brought about by:
- not taking your Humalog or other insulin;
- taking less insulin than your doctor tells you to;
- eating a lot more than your diet allows; or
- fever, infection or emotional stress.

Hyperglycaemia can lead to diabetic ketoacidosis. The first symptoms come on slowly over many hours or days. The symptoms include the following:
- feeling sleepy
- flushed face
- thirst
- no appetite
- fruity smell on the breath
- feeling or being sick

Severe symptoms are heavy breathing and a rapid pulse. **Get medical help immediately.**

C. Illness
If you are ill, especially if you feel sick or are sick, the amount of insulin you need may change. **Even when you are not eating normally, you still need insulin.** Test your urine or blood, follow your 'sick rules', and tell your doctor.

5. How to store Humalog Tempo Pen

Before the first use store your Humalog Tempo Pen in a refrigerator (2°C – 8°C). Do not freeze.

Keep your Humalog Tempo Pen in use at room temperature (below 30°C) and discard after 28 days even if some of the solution remains. Do not put it near heat or in the sun. Do not keep the Tempo Pen that you are using in the fridge. The Tempo Pen should not be stored with the needle attached.

Keep out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the label and the carton. The expiry date refers to the last day of that month.

Do not use this medicine if you notice the solution is coloured or it has solid pieces in it. You must use it **only** if it looks like water. Check this each time you inject yourself.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. Contents of the pack and other information

What Humalog 100 units/ml Tempo Pen solution for injection contains
- The active substance is insulin lispro. Each ml of solution contains 100 units (U) of insulin lispro. Each pre-filled pen (3 ml) contains 300 units (U) of insulin lispro.
- The other ingredients are metacresol, glycerol, dibasic sodium phosphate 7 H_2O, zinc oxide and water for injections. Sodium hydroxide or hydrochloric acid may have been used to adjust the acidity.

What Humalog Tempo Pen looks like and contents of the pack
Humalog 100 units/ml Tempo Pen solution for injection is a sterile, clear, colourless, aqueous solution and contains 100 units of insulin lispro in each millilitre (100 units/ml) solution for injection. Each Humalog Tempo Pen contains 300 units (3 millilitres). The Humalog Tempo Pen comes in a pack of 5 pre-filled pens or a multipack of 2 x 5 pre-filled pens. Not all pack sizes may be marketed. The Humalog 100 units/ml in your pre-filled pen is the same as the Humalog 100 units/ml, which comes in separate Humalog 100 units/ml cartridges. The pre-filled pen simply has a built in cartridge. When the pre-filled pen is empty you cannot use it again. The Tempo Pen contains a magnet (see section 2, "Warnings and precautions").

Marketing Authorisation Holder

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Manufacturer

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This leaflet was last revised in

Detailed information on this medicine is available on the European Medicines Agency web site: https://www.ema.europa.eu.

Instructions for use

Humalog 100 units/ml Tempo Pen solution for injection in a pre-filled pen
insulin lispro



PLEASE READ THESE INSTRUCTIONS BEFORE USE

Read the instructions for use before you startusing your insulin and each time you get another Humalog Tempo Pen. There may be new information. This information does not take the place of talking to your healthcare professional about your medical condition or your treatment.

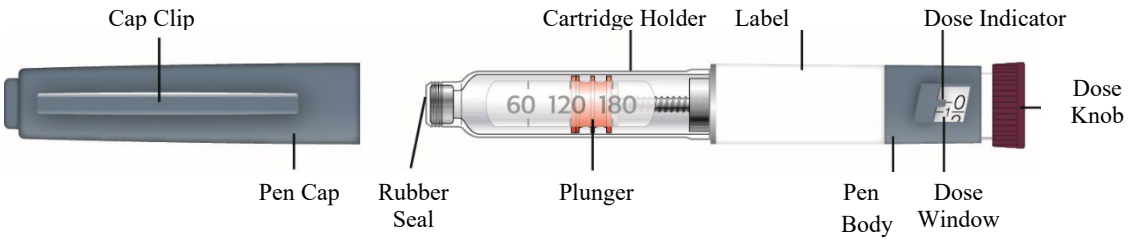
Tempo Pen ("Pen") is a disposable prefilled Pen containing 3 ml (300 units, 100 units/ml) of insulin. You can give yourself multiple doses using one Pen. The Pen dials 1 unit at a time. You can give from 1 to 60 units in a single injection. **If your dose is more than 60 units, you will need to give yourself more than one injection.** The plunger only moves a little with each injection, and you may not notice that it moves. The plunger will only reach the end of the cartridge when you have used all 300 units in the Pen.

The Tempo Pen is designed to work with the Tempo Smart Button. The Tempo Smart Button is an optional product that can be attached to the Tempo Pen dose knob and aids in transmitting Humalog dose information from the Tempo Pen to a compatible mobile application. The Tempo Pen injects insulin with or without the Tempo Smart Button attached. Your Smart Button must be attached to a Tempo Pen to record or transfer dose data. Push the Smart Button straight down on the dose knob until you hear a snap or feel the Smart Button snap into place. To transmit data to the mobile application, follow the instructions provided with the Tempo Smart Button and the instructions with the mobile application.

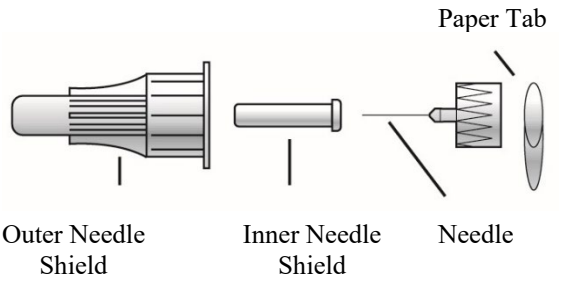
Do not share your Pen with other people, even if the needle has been changed. Do not reuse or share needles with other people. You may give an infection to them or get an infection from them.

This Pen is not recommended for use by the blind or visually impaired without the help of someone trained to use the Pen.

Tempo Pen Parts



Pen Needle Parts
(Needles Not Included)



How to recognize your Tempo Pen:

- Pen colour: Blue
- Dose Knob: Burgundy
- Labels: White with Burgundy colour bar

Supplies needed to give your injection:

- Tempo Pen containing your insulin
- Tempo Pen compatible Needle (BD [Becton, Dickinson and Company] Pen Needles recommended)
- Swab

Needles and swab are not included

Preparing your Pen

- Wash your hands with soap and water.
- Check the Pen to make sure you are taking the right type of insulin. This is especially important if you use more than 1 type of insulin.
- **Do not** use your Pen past the expiration date printed on the label. After you start using the Pen, throw your Pen away after the in-use time specified in the package leaflet.
- Always use a **new needle** for each injection to help prevent infections and blocked needles.

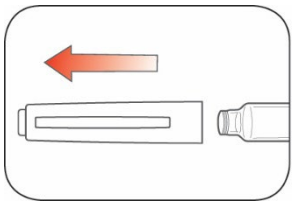
Step 1:

- Pull the Pen cap straight off.

– **Do not** remove the Pen label.

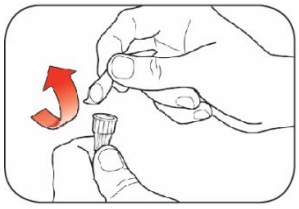
- Wipe the rubber seal with a swab.

HUMALOG should look clear and colourless. Do not use if it is cloudy, coloured, or has particles or clumps in it.



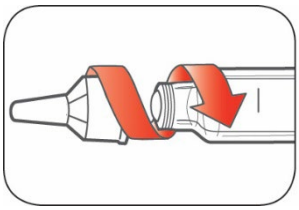
Step 2:

- Select a new needle.
- Pull off the paper tab from the outer needle shield.



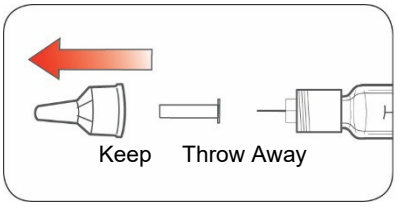
Step 3:

- Push the capped needle straight onto the Pen and twist the needle on until it is tight.



Step 4:

- Pull off the outer needle shield. **Do not** throw it away.
- Pull off the inner needle shield and throw it away.



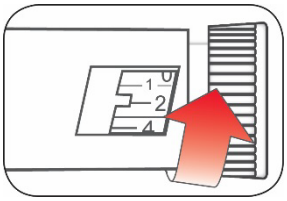
Priming your Pen

Prime before each injection.

- Priming your Pen means removing the air from the needle and cartridge that may collect during normal use and ensures that the Pen is working correctly.
- If you **do not** prime before each injection, you may get too much or too little insulin.

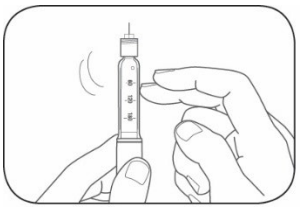
Step 5:

- To prime your Pen, turn the dose knob to select 2 units.



Step 6:

- Hold your Pen with the needle pointing up. Tap the cartridge holder gently to collect air bubbles at the top.



Step 7:

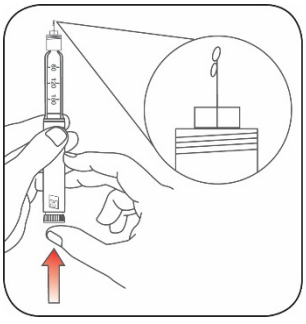
- Continue holding your Pen with needle pointing up. Push the dose knob in until it stops, and "0" is seen in the dose window. Hold the dose knob in and count to 5 slowly.

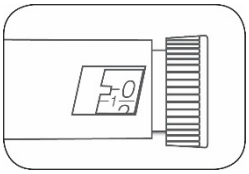
  You should see insulin at the tip of the needle.

– If you **do not** see insulin, repeat the priming steps, but not more than 4 times.

– If you **still do not** see insulin, change the needle and repeat the priming steps.

Small air bubbles are normal and will not affect your dose.



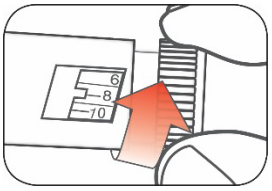


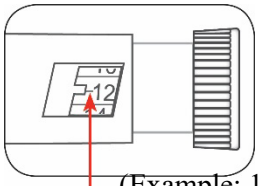
Selecting your dose

- You can give from 1 to 60 units in a single injection.
- If your dose is more than 60 units, you will need to give more than one injection.
  - If you need help deciding how to divide up your dose, ask your healthcare professional.
    - You should use a new needle for each injection and repeat the priming step.

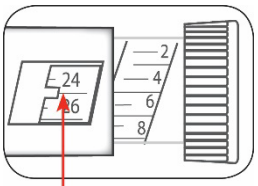
Step 8:

- Turn the dose knob to select the number of units you need to inject. The dose indicator should line up with your dose.
  - The Pen dials 1 unit at a time.
  - The dose knob clicks as you turn it.
  - **DO NOT** dial your dose by counting the clicks because you may dial the wrong dose.
  - The dose can be corrected by turning the dose knob in either direction until the correct dose lines up with the dose indicator.
  - The even numbers are printed on the dial.
  - The odd numbers, after the number 1, are shown as full lines.
- **Always check the number in the dose window to make sure you have dialed the correct dose.**





(Example: 12 units shown in the dose window)



(Example: 25 units shown in the dose window)

- The Pen will not let you dial more than the number of units left in the Pen.
- If you need to inject more than the number of units left in the Pen, you may either:
  - inject the amount left in your Pen and then use a new Pen to give the rest of your dose, **or**
  - get a new Pen and inject the full dose.
- It is normal to see a small amount of insulin left in the Pen that you cannot inject.

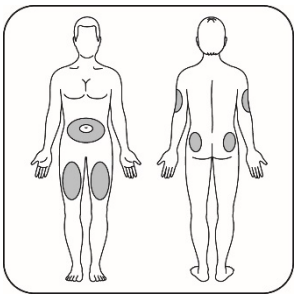
Giving your injection

- Inject your insulin as your healthcare professional has shown you.
- Change (rotate) your injection site for each injection.
- **Do not** try to change your dose while injecting.

Step 9:

- Choose your injection site.

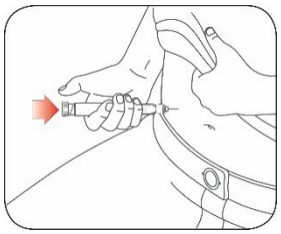
  Your insulin is injected under the skin (subcutaneously) of your stomach area, buttocks, upper legs or upper arms.
- Wipe the skin with a swab, and let the injection site dry before you inject your dose.



Step 10:

- Insert the needle into your skin.
- Push the dose knob all the way in.
- Continue to hold the Dose knob in and **slowly count to 5** before removing the needle.

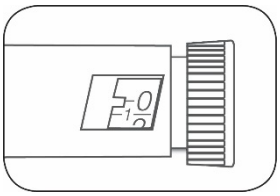




Do not try to inject your insulin by turning the dose knob. You will **NOT** receive your insulin by turning the dose knob.

Step 11:

- Pull the needle out of your skin.
  - A drop of insulin at the needle tip is normal. It will not affect your dose.
- Check the number in the dose window
  - If you see “0” in the dose window, you have received the full amount you dialed.
  - If you do not see “0” in the dose window, do not redial. Insert the needle into your skin and finish your injection.
  - If you **still** do not think you received the full amount you dialed for your injection**, do not start over or repeat that injection.** Monitor your blood glucose as instructed by your healthcare professional.
  - If you normally need to give 2 injections for your full dose, be sure to give your second injection.

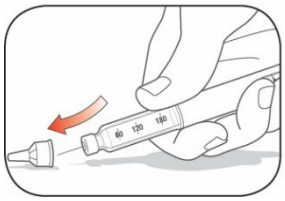


The plunger only moves a little with each injection, and you may not notice that it moves.

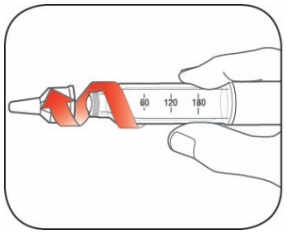
If you see blood after you take the needle out of your skin, press the injection site lightly with a piece of gauze or a swab. **Do not** rub the area.

After your injection

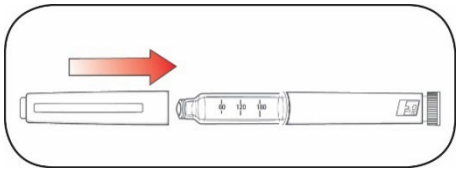
Step 12:
- Carefully replace the outer needle shield.



Step 13:
- Unscrew the capped needle and dispose of it as described below (see **disposing of Pens and needles** section).
- Do not store the Pen with the needle attached to prevent leaking, blocking the needle, and air from entering the Pen.



Step 14:
- Replace the Pen cap by lining up the cap clip with the dose indicator and pushing straight on.



Disposing of Pens and Needles

- Put used needles in a sharps container or a hard plastic container with a secure lid. **Do not** throw needles directly into your household waste.
- **Do not** recycle the filled sharps container.
- Ask your healthcare professional about options to dispose of the pens and the sharps container properly.
- The directions regarding needle handling are not intended to replace local, healthcare professional or institutional policies.

Storing your Pen

Unused Pens
- Store unused Pens in the refrigerator at 2°C to 8°C.
- **Do not** freeze your insulin. **Do not** use if it has been frozen.
- Unused Pens may be used until the expiration date printed on the label, if the Pen has been kept in the refrigerator.

In-use Pen
- Store the Pen you are currently using at room temperature (below 30°C) and away from dust, food and liquids, heat and light.
- Throw away the Pen you are using after the time specified in the package leaflet, even if it still has insulin left in it.

General information about the safe and effective use of your Pen

- **Keep your Pen and needles out of the sight and reach of children.**
- **Do not** use your Pen if any part looks broken or damaged.
- Always carry an extra Pen in case yours is lost or damaged.

Troubleshooting

- If you cannot remove the Pen cap, gently twist the cap back and forth, and then pull the cap straight off.
- If the dose knob is hard to push:

– Pushing the dose knob more slowly will make it easier to inject.

– Your needle may be blocked. Put on a new needle and prime the Pen.

– You may have dust, food, or liquid inside the Pen. Throw the Pen away and get a new Pen. You may need to get a prescription from your healthcare professional.

If you have any questions or problems with your Tempo Pen, contact your healthcare professional for help or contact your local Lilly affiliate.

Document revision date: