ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Roclanda 50 micrograms/ml + 200 micrograms/ml eye drops, solution

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml of solution contains 50 micrograms latanoprost and 200 micrograms netarsudil (as mesylate).

Excipient with known effect

Each ml of solution contains 200 micrograms benzalkonium chloride.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Eye drops, solution (eye drops).

Clear, colourless solution, pH 5 (approximately).

Osmolality: 280 mOsm/Kg.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Roclanda is indicated for the reduction of elevated intraocular pressure (IOP) in adult patients with primary open-angle glaucoma or ocular hypertension for whom monotherapy with a prostaglandin or netarsudil provides insufficient IOP reduction.

4.2 Posology and method of administration

Treatment with Roclanda should only be initiated by an ophthalmologist or a healthcare professional qualified in ophthalmology.

Posology

The recommended dose is one drop in the affected eye(s) once daily in the evening. Patients should not instil more than one drop in the affected eye(s) each day.

If one dose is missed, treatment should continue with the next dose in the evening.

Paediatric population
The safety and efficacy of Roclanda in children below the age of 18 years have not been established. No data are available.

Method of administration

For ocular use.

Data on potential interactions specific to latanoprost + netarsudil are described in section 4.5. If latanoprost + netarsudil is to be used concomitantly with other topical ophthalmic medicinal products, each medicinal product should be administered at least five minutes apart. Due to netarsudil's

vasodilating properties, other eye drops should be administered before latanoprost + netarsudil. Eye ointments should be administered last.

Contact lenses should be removed prior to instillation of latanoprost + netarsudil and may be reinserted 15 minutes following its administration (see section 4.4).

As with any eye drops, to reduce possible systemic absorption, it is recommended that the lachrymal sac be compressed at the medial canthus (punctal occlusion) for one minute. This should be performed immediately following the instillation of each drop.

The tip of the dispensing container should avoid contacting the eye, surrounding structures, fingers, or any other surface in order to avoid contamination of the solution. Serious damage to the eye and subsequent loss of vision may result from using contaminated solutions.

4.3 Contraindications

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

4.4 Special warnings and precautions for use

Iris pigmentation

Latanoprost may gradually change eye colour by increasing the amount of brown pigment in the iris. Before treatment is instituted, patients should be informed of the possibility of a permanent change in eye colour. Unilateral treatment can result in permanent heterochromia.

Increased iris pigmentation has not been shown to have any negative clinical sequelae and treatment with medicinal products containing latanoprost can be continued if iris pigmentation ensues. However, patients should be monitored regularly and if the clinical situation warrants, treatment with medicinal products containing latanoprost may be discontinued.

Herpetic keratitis condition

Medicinal product(s) containing latanoprost should be used with caution in patients with a history of herpetic keratitis, and should be avoided in cases of active herpes simplex keratitis and in patients with a history of recurrent herpetic keratitis specifically associated with prostaglandin analogues.

Macular oedema risk

Reports of macular oedema with medicinal products containing latanoprost have occurred mainly in aphakic patients, in pseudophakic patients with torn posterior lens capsule or anterior chamber lenses, or in patients with known risk factors for cystoid macular oedema (such as diabetic retinopathy and retinal vein occlusion). Medicinal products containing latanoprost should be used with caution in aphakic patients, in pseudophakic patients with torn posterior lens capsule or anterior chamber lenses, or in patients with known risk factors for cystoid macular oedema.

Iritis/uveitis risk

In patients with known predisposing risk factors for iritis/uveitis, medicinal products containing latanoprost can be used with caution.

Asthma exacerbation

There is limited experience of latanoprost use in patients with asthma, but some cases of exacerbation of asthma and/or dyspnoea were reported in post marketing experience. Asthmatic patients should therefore be treated with caution until there is sufficient experience with the combination.

Periorbital skin discolouration

Periorbital skin discolouration has been observed on treatment with medicinal products containing latanoprost, the majority of reports being in Japanese patients. Experience to date shows that periorbital skin discolouration is not permanent and in some cases has reversed while continuing treatment with latanoprost.

Eyelash changes

Treatment with medicinal products containing latanoprost may gradually change eyelashes and vellus hair in the treated eye and surrounding areas; these changes include increased length, thickness, pigmentation, number of lashes or hairs and misdirected growth of eyelashes. Eyelash changes are reversible upon discontinuation of treatment.

Reticular epithelial corneal oedema

Reticular epithelial corneal oedema (RECE) has been reported following administration of medicinal products containing netarsudil, particularly in patients with preexisting corneal oedema or prior ocular surgery. RECE typically resolves upon discontinuation of the medicinal product containing netarsudil. Patients should be advised to notify their physician if they experience decreased vision or eye pain while using Roclanda.

The efficacy of Roclanda has not been studied beyond 12 months.

Excipient with known effect

Benzalkonium chloride
This medicinal product contains benzalkonium chloride.

Benzalkonium chloride has been reported to cause eye irritation, symptoms of dry eyes and may affect the tear film and corneal surface and is known to discolour soft contact lenses. It should be used with caution in dry eye patients and in patients where the cornea may be compromised.
Patients should be monitored in case of prolonged use.

4.5 Interaction with other medicinal products and other forms of interaction

In vitro interaction studies have shown that precipitation can occur when eye drops containing thiomersal are mixed with latanoprost + netarsudil. Administer other eye drops at least five minutes apart (see section 4.2).

In vitro studies have indicated netarsudil has the potential to inhibit CYP450 isoenzymes in the cornea, however no clinical evidence of local pharmacokinetic interactions has been observed to date.

There have been reports of paradoxical elevations in IOP following the concomitant ophthalmic administration of two prostaglandin analogues. Therefore, the use of two or more prostaglandins, prostaglandin analogues or prostaglandin derivatives is not recommended.

4.6 Fertility, pregnancy and lactation

Pregnancy

There are no or limited amount of data from the use of latanoprost + netarsudil in pregnant women.

No effects during pregnancy are anticipated, since systemic exposure to netarsudil is negligible (see section 5.2). Animal studies with intravenous administration of netarsudil do not indicate direct or

indirect harmful effects with respect to reproductive toxicity at clinically relevant exposures (see section 5.3).

Latanoprost has potentially harmful pharmacological effects during pregnancy and/or on the fetus/newborn child (see section 5.3).

Therefore, latanoprost + netarsudil should not be used during pregnancy.

Breast-feeding

It is unknown whether netarsudil/metabolites are excreted in human milk. However, while no effects on the breastfed newborn/infant are anticipated since the systemic exposure of breast-feeding women to netarsudil is expected to be negligible, no relevant clinical data are available (see section 5.2).

Latanoprost and its metabolites may pass into human milk. A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from Roclanda therapy taking into account the benefit of breast feeding for the child and the benefit of therapy for the woman.

Fertility

There are no data on the effects of netarsudil on male or female fertility. However, no effects are anticipated, since systemic exposure to netarsudil is negligible (see section 5.2). Latanoprost has not been found to have any effect on male or female fertility in animal studies (see section 5.3).

4.7 Effects on ability to drive and use machines

Roclanda has negligible influence on the ability to drive and use machines.

If transient blurred vision occurs at instillation, the patient should wait until the vision clears before driving or using machines.

4.8 Undesirable effects

Summary of the safety profile

The most common adverse reactions observed in the clinical studies were conjunctival hyperaemia (46% of patients), instillation site pain (14%), cornea verticillata (12%) and eye pruritis (7%). Serious adverse reactions were not reported in clinical studies.

Tabulated list of adverse reactions

The following adverse reactions have been reported with latanoprost + netarsudil, dosed once daily, and during clinical studies and post-marketing surveillance with the individual components latanoprost and netarsudil. Adverse reactions are presented according to the MedDRA system organ classification. Within each system organ class, the adverse reactions are classified by frequency according to the following convention: 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) or not known (cannot be estimated from the available data).

System organ classification	**Frequency**	**Adverse reactions**
Infections and infestations	Rare	Herpetic keratitis[2]
Immune system disorders	Uncommon	Hypersensitivity
Nervous system disorders	Uncommon	Headache, Muscle contractions involuntary, Dizziness, Visual field defect[3]

System organ classification	Frequency	Adverse reactions
Eye disorders	Very common	Conjunctival hyperaemia[1], Cornea verticillata[1], Instillation site pain, Iris hyperpigmentation[2], Eyelash and vellus hair changes of the eyelid (increased length, thickness, pigmentation and number of eyelashes)[2]
	Common	Conjunctival haemorrhage, Vision blurred, Lacrimation increased, Erythema of eyelid, Eye pruritus, Eye irritation, Visual acuity reduced, Eyelid oedema, Punctate keratitis, Corneal disorder, Conjunctival oedema, Conjunctivitis allergic, Eye pain, Dry eye, Foreign body sensation in eyes, Eyelid margin crusting, Blepharitis, Instillation site erythema, Instillation site discomfort, Vital dye staining cornea present
	Uncommon	Eyelids pruritus, Conjunctival disorder, Corneal opacity, Eye discharge, Corneal deposits, Conjunctivitis, Dacryostenosis acquired, Eye inflammation, Eye paraesthesia, Conjunctival follicles, Eye swelling, Meibomian gland dysfunction, Corneal pigmentation, Diplopia, Noninfective conjunctivitis, Abnormal sensation in eye, Keratitis, Refraction disorder, Anterior chamber flare, Conjunctival irritation, Intraocular pressure increased, Eyelid rash, Eyelid skin dryness, Growth of eyelashes, Lacrimal disorder, Iritis, Visual impairment, Corneal dystrophy,

System organ classification	Frequency	Adverse reactions
		Instillation site dryness, Instillation site pruritus, Instillation site reaction, Eye complication associated with device, fatigue, Instillation site paraesthesia, Macular oedema including cystoid macular oedema[2], Uveitis[2] Ocular hyperaemia Diabetic retinopathy[3], Eye allergy[3] Ocular discomfort, Eyelid disorder[3], Ectropion[3], Lenticular opacities[3], Asthenopia[3], Episcleral hyperaemia[3], Halo vision[3], Anterior chamber inflammation[3], Blindness[3], Conjunctivochalasis, Eczema eyelids[3], Glaucoma[3], Iris adhesions[3], Iris bombe[3], Ocular hypertension[3], Instillation site irritation[3], Glassy eyes[3], Instillation site oedema[3], Conjunctival staining[3], Optic nerve cup/disc ratio increased[3], Madarosis[3], Blepharal pigmentation, Eye disorder, Retinal haemorrhage, Photophobia
	Rare	Corneal oedema[2], Corneal erosion[2], Periorbital oedema[2], Trichiasis[2], Distichiasis[2], Iris cyst[2], Localised skin reaction on the eyelids[2], Darkening of the palpebral skin of the eyelids[2], Pseudopemphigoid of ocular conjunctiva[2]
	Very rare	Periorbital and lid changes resulting in deepening of the eyelid sulcus[2]
	Not known	Reticular epithelial corneal oedema[3]
Cardiac disorders	Uncommon	Angina[2], Palpitations[2]
	Very rare	Angina unstable[2]
	Uncommon	Epistaxis,

System organ classification	Frequency	Adverse reactions
Respiratory, thoracic and mediastinal disorders		Nasal congestion, Nasal discomfort[3], Rhinalgia[3] Asthma[2], Dyspnoea[2]
	Rare	Asthma exacerbation[2]
Gastrointestinal disorders	Uncommon	Nausea, Vomiting
Skin and subcutaneous tissue disorders	Common	Dermatitis contact
	Uncommon	Lichenification, Dry skin, Erythema, Skin disorder, Dermatitis allergic[3] Petechiae, Eczema
	Rare	Pruritus[2]
Musculoskeletal and connective tissue disorders	Uncommon	Pain in jaw, Myalgia[2], Arthralgia[2], Polychondritis[3], Muscular weakness, Sjogren's syndrome
General disorders and administration site conditions	Uncommon	Chest pain[2]
Injury, poisoning and procedural complications	Uncommon	Excoriation[3]

[1] See *Description of selected adverse reactions* for further information
[2] Additional adverse reaction observed with latanoprost monotherapy
[3] Additional adverse reaction observed with netarsudil monotherapy

Description of selected adverse reactions

Conjunctival hyperaemia
Conjunctival hyperaemia was the most frequently reported adverse reaction associated with latanoprost + netarsudil treatment in clinical studies and it is attributed to the vasodilation effect of the Rho kinase inhibitor medicinal product class. Conjunctival hyperaemia was typically mild in severity and sporadic. However, there was a relatively small proportion of subjects with moderate or severe hyperaemia who discontinued treatment because of this adverse reaction (5% in Phase 3 clinical studies).

Cornea verticillata
Cornea verticillata occurred in approximately 13% of the patients in controlled Phase 3 clinical studies. The cornea verticillata seen in latanoprost + netarsudil-treated patients were first noted at 4 weeks of daily dosing. This reaction did not result in any apparent visual functional changes in patients. The majority of cornea verticillata resolved upon discontinuation of treatment. The incidence of cornea verticillata was higher in certain subpopulations: elderly (≥65 years) versus non-elderly (18.8 vs. 11.5%); males versus females (18.8 vs. 13.0%) and in white versus other races (21.7 vs. 2.5%).

Iris pigmentation
Roclanda contains latanoprost which is a prostaglandin F2α analogue. The majority of adverse reactions associated with latanoprost are ocular in nature. In a 5-year latanoprost safety study, 33% of patients developed iris pigmentation (section 4.4).

This change in eye colour has predominantly been seen in patients with mixed coloured irides, i.e. blue-brown, grey-brown, yellow-brown and green-brown. In studies with latanoprost, the onset of the change is usually within the first 8 months of treatment, rarely during the second or third year, and has

not been seen after the fourth year of treatment. The rate of progression of iris pigmentation decreases with time and is stable for five years. The effect of increased pigmentation beyond five years has not been evaluated. The iris colour change is slight in the majority of cases and often not observed clinically. The incidence in patients with mixed colour irides ranged from 7 to 85%, with yellow-brown irides having the highest incidence. In patients with homogeneously blue eyes, no change has been observed and in patients with homogeneously grey, green or brown eyes, the change has only rarely been seen.

The colour change is due to increased melanin content in the stromal melanocytes of the iris and not to an increase in number of melanocytes. Typically, the brown pigmentation around the pupil spreads concentrically towards the periphery in affected eyes, but the entire iris or parts of it may become more brownish. No further increase in brown iris pigment has been observed after discontinuation of treatment. It has not been associated with any symptom or pathological changes in clinical studies to date.

Neither naevi nor freckles of the iris have been affected by treatment. Accumulation of pigment in the trabecular meshwork or elsewhere in the anterior chamber has not been observed in clinical studies.

Other special populations

Elderly
With the exception of cornea verticillata (see above), no difference in the safety profile for latanoprost + netarsudil has been observed between subjects aged < 65 or ≥ 65 years.

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

Systemic exposure to the netarsudil component of latanoprost + netarsudil following topical ocular administration has been shown to be negligible.

Apart from ocular irritation and conjunctival hyperaemia, no other ocular side effects are known if latanoprost is overdosed.

If latanoprost is accidentally ingested the following information may be useful: one bottle contains 125 micrograms latanoprost. More than 90% is metabolised during the first pass through the liver. Intravenous infusion of 3 micrograms/kg in healthy volunteers induced no symptoms, but a dose of 5.5-10 micrograms/kg caused nausea, abdominal pain, dizziness, fatigue, hot flushes and sweating. In monkeys, latanoprost has been infused intravenously in doses of up to 500 micrograms/kg without major effects on the cardiovascular system.

Intravenous administration of latanoprost in monkeys has been associated with transient bronchoconstriction. However, in patients with moderate bronchial asthma, bronchoconstriction was not induced by latanoprost when applied topically on the eyes in a dose of seven times the clinical dose of latanoprost.

If topical overdose of latanoprost + netarsudil should occur, the eye(s) may be flushed with tap water. Treatment of an overdose would include supportive and symptomatic therapy.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Ophthalmologicals, antiglaucoma preparations and miotics, ATC code: S01EE51

Mechanism of action

Roclanda contains two active substances: latanoprost and netarsudil. These two components lower IOP by increasing the outflow of aqueous humor. Although both latanoprost and netarsudil lower IOP by increasing aqueous humor outflow, their mechanisms of action are different.

Studies in animal and man suggest that the main mechanism of action for netarsudil, a Rho kinase inhibitor, is increased trabecular outflow. These studies also suggest that netarsudil lowers IOP by reducing episcleral venous pressure.

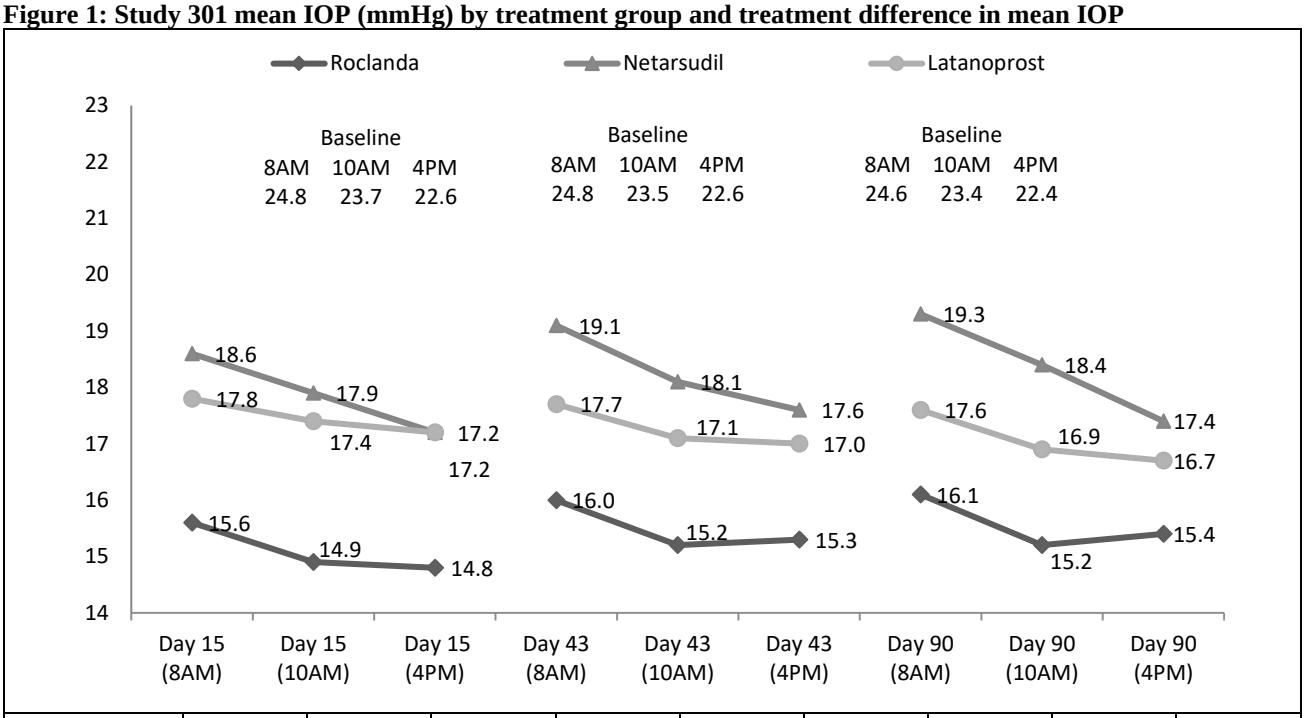
Studies in animal and man indicate that the main mechanism of action for latanoprost, a prostaglandin F2α analoque, is increased uveoscleral outflow, although some increase in outflow facility (decrease in outflow resistance) has been reported in man.

Clinical efficacy and safety

Roclanda was evaluated in 3 randomized, double-blind, multicentre Phase 3 clinical studies in 1 686 patients with open-angle glaucoma and ocular hypertension. Studies 301 and 302 enrolled subjects with IOP < 36 mmHg and compared IOP lowering effect of latanoprost + netarsudil dosed once daily to individually administered netarsudil 0.02% once daily and latanoprost 0.005% once daily. The treatment duration was 12 months for Study 301 and 3 months for Study 302. The median age of study participants was 66 years (range 18 to 99 years). Study 303 assessed the ocular hypotensive efficacy of latanoprost + netarsudil relative to bimatoprost 0.03%/timolol 0.5%. The treatment duration was 6 months.

Studies 301 and 302 were designed to show superiority of latanoprost + netarsudil when dosed once daily in the evening over its individual components netarsudil 0.02% once daily and latanoprost 0.005% once daily. The primary efficacy outcome measure was least squares (LS) mean IOP at each of 9 timepoints measured at 08:00, 10:00 and 16:00 on day 15, day 43 and day 90. The average IOP lowering effect of latanoprost + netarsudil was 1 to 3 mmHg greater than monotherapy with either netarsudil 0.02% or latanoprost 0.005% throughout 3 months (Figures 1 and 2). In Study 301 IOP reductions were maintained, showing statistical superiority of latanoprost + netarsudil throughout the 12-month treatment period. In all cases, the differences in the LS mean IOP were clinically relevant and statistically significant ($p < 0.0001$) through month 3. Approximately 30% of subjects included in the Phase 3 studies had a baseline IOP of ≥ 27 mmHg (132, 136 and 143 in the latanoprost + netarsudil, latanoprost and netarsudil treatment groups, respectively). In these subjects, latanoprost + netarsudil showed statistically significantly superior IOP-lowering efficacy to each of its components at all time points. Across both studies, compared to latanoprost alone, the combination product reduced IOP by a further 1.7 mmHg to 3.7 mmHg, and compared to netarsudil alone by a further 3.4 mmHg to 5.9 mmHg.

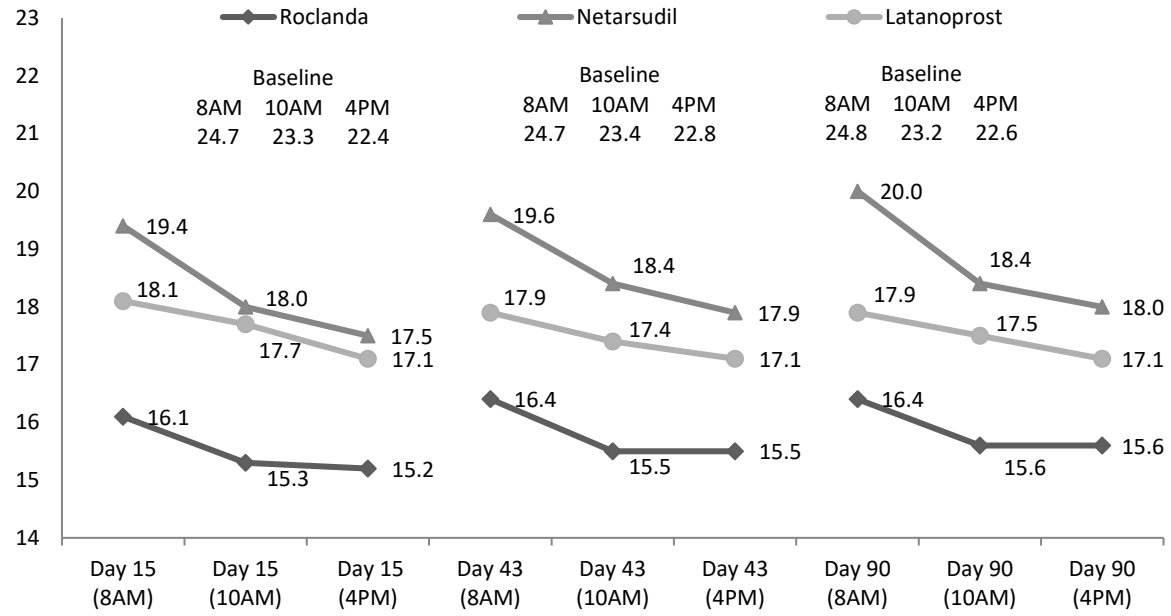
Figure 1: Study 301 mean IOP (mmHg) by treatment group and treatment difference in mean IOP



latanoprost + netarsudil vs. netarsudil 95% CI	**3.0 (2.5, 3.6)**	**3.0 (2.4, 3.6)**	**2.4 (1.9, 3.0)**	**3.2 (2.6, 3.8)**	**2.9 (2.3, 3.5)**	**2.3 (1.7, 2.8)**	**3.1 (2.5, 3.8)**	**3.2 (2.5, 3.8)**	**2.0 (1.4, 2.6)**
latanoprost + netarsudil vs. latanoprost 95% CI	**2.3 (1.7, 2.8)**	**2.6 (2.0, 3.2)**	**2.3 (1.8, 2.9)**	**1.7 (1.1, 2.4)**	**1.9 (1.3, 2.5)**	**1.7 (1.1, 2.2)**	**1.5 (0.9, 2.1)**	**1.7 (1.1, 2.3)**	**1.3 (0.7, 1.9)**

The LS mean IOP at each post-baseline time point was derived using an analysis of covariance adjusted for baseline IOP and based on observed data for all randomized subjects (238 in latanoprost + netarsudil group, 244 in netarsudil group, 236 in latanoprost group).

Figure 2: Study 302 mean IOP (mmHg) by treatment group and treatment difference in mean IOP



latanoprost + netarsudil vs. netarsudil 95% CI	**3.4 (2.8, 3.9)**	**2.7 (2.2, 3.2)**	**2.2 (1.7, 2.8)**	**3.2 (2.6, 3.8)**	**2.9 (2.3, 3.4)**	**2.3 (1.8, 2.9)**	**3.6 (3.0, 4.2)**	**2.8 (2.3, 3.4)**	**2.4 (1.9, 2.9)**
latanoprost + netarsudil vs. latanoprost 95% CI	**2.0 (1.5, 2.6)**	**2.4 (1.9, 2.9)**	**1.9 (1.3, 2.4)**	**1.5 (0.9, 2.1)**	**1.9 (1.3, 2.4)**	**1.6 (1.0, 2.1)**	**1.5 (0.9, 2.2)**	**2.0 (1.4, 2.5)**	**1.5 (1.0, 2.1)**

The LS mean IOP at each post-baseline time point was derived using an analysis of covariance adjusted for baseline IOP and based on observed data for all randomized subjects (245 in latanoprost + netarsudil group, 255 in netarsudil group, 250 in latanoprost group).

Approximately 67% of subjects included in the latanoprost + netarsudil treatment groups of Phase 3 studies were caucasian and 30% black or african american. Over half were aged ≥ 65 years. With the exception of the incidence of cornea verticillata (section 4.8); no other difference in safety profile was observed between races or age groups.

Completion rates in studies 301 and 302 were lower in the latanoprost + netarsudil treatment groups when compared with the latanoprost group. Discontinuation rates due to adverse events at month 3 were 8.7% for the pooled latanoprost + netarsudil treatment group versus 7.6% for the pooled netarsudil group and 1.0% for the pooled latanoprost group. Discontinuation rates due to adverse events at month 12 in Study 301 were 19.7% for the latanoprost + netarsudil treatment group versus 21.7% for the netarsudil group and 1.7% for the latanoprost group. The majority of discontinuations were associated with ocular events. The most frequently reported adverse event associated with discontinuation in the latanoprost + netarsudil group was conjunctival hyperemia (7.6% at month 12). The majority of ocular adverse events reported with netarsudil + latanoprost were mild in intensity.

Study 303 was a prospective, double-masked, randomized, multicenter, active-controlled, parallel-group, 6-month study assessing the safety and ocular hypotensive efficacy of latanoprost + netarsudil compared to bimatoprost + timolol in 430 subjects with elevated intraocular pressure. Subjects were randomly assigned to a planned fixed-dose treatment regimen with latanoprost + netarsudil one drop (218 subjects), once daily (QD) each evening in both eyes (OU) or comparator bimatoprost + timolol (212 subjects) one drop QD each evening OU for approximately 180 days following a washout period.

The primary efficacy outcome was the comparison of latanoprost + netarsudil to bimatoprost + timolol for Mean IOP at specified timepoints at Week 2, Week 6, and Month 3. The primary analysis was

performed on the ITT population with imputation by Markov Chain Monte Carlo (MCMC) method. This analysis demonstrated clinical non-inferiority of latanoprost + netarsudil ophthalmic solution relative to bimatoprost + timolol dosed QD in the ITT population with the upper limit of the 95% CIs around the difference (latanoprost + netarsudil - bimatoprost + timolol) ≤ 1.5 mmHg at all 9 time points and ≤ 1.0 mmHg at the majority (6 out of 9) of time points from Week 2 through Month 3, meeting the criteria for success. The threshold for clinical non-inferiority of latanoprost + netarsudil QD relative to bimatoprost + timolol QD (the between-group difference ≤ 1.5 mmHg) was demonstrated in the PP population at 8 out of 9 time points (08:00, 10.00, and 16:00) at week 2, through month 3 using the MCMC method. However, clinical non inferiority was not met overall since at the week 6 08:00 time point, the upper bound 95% CI was 1.55. Overall, there was a similar mean IOP reduction throughout the day of approximately 9.5 mmHg between both the latanoprost + netarsudil and bimatoprost + timolol treatment group.

The overall rate of discontinuation from the study treatment due to a TEAE was 11.2%. More subjects in the latanoprost + netarsudil QD treatment group discontinued from the study treatment due to a TEAE (20.2%) compared to the bimatoprost + timolol QD group (1.9%), and the majority of TEAEs leading to discontinuation were ocular TEAEs. No serious treatment-related adverse events were reported in any treatment group, and the safety profile remains consistent with the known profile for latanoprost + netarsudil, and/or latanoprost or netarsudil alone.

The efficacy and safety of latanoprost + netarsudil in subjects with compromised corneal epithelium or co-existing ocular pathologies e.g. pseudoexfoliation and dispersion pigment syndrome has not been established.

Paediatric population

The European Medicines Agency has waived the obligation to submit the results of studies with Roclanda in all subsets of the paediatric population for the reduction of elevated intraocular pressure in patients with open-angle glaucoma or ocular hypertension (see section 4.2 for information on paediatric use).

5.2 Pharmacokinetic properties

Absorption

The systemic exposures of netarsudil and its active metabolite, AR-13503, were evaluated in 18 healthy subjects after topical ocular administration of netarsudil 200 micrograms/ml once daily (one drop bilaterally in the morning) for 8 days. There were no quantifiable plasma concentrations of netarsudil (lower limit of quantitation (LLOQ) 0.100 ng/ml) post dose on Day 1 and Day 8. Only one plasma concentration at 0.11 ng/ml for the active metabolite was observed for one subject on Day 8 at 8 hours post-dose.

Latanoprost (molecular weight 432.58) is an isopropyl ester prodrug which per se is inactive, but after hydrolysis to the acid of latanoprost becomes biologically active. The prodrug is well absorbed through the cornea and all active substance that enters the aqueous humour is hydrolysed during the passage through the cornea. Studies in man indicate that the peak concentration in the aqueous humour is reached about two hours after topical administration. After topical application in monkeys, latanoprost is distributed primarily in the anterior segment, the conjunctivae and the eyelids. Only minute quantities of latanoprost reach the posterior segment.

Biotransformation

After topical ocular dosing, netarsudil is metabolized by esterases in the eye to an active metabolite, AR-13503.

There is practically no metabolism of the acid of latanoprost in the eye. The main metabolism occurs in the liver. The half-life in plasma is 17 minutes in man. The main metabolites, the 1,2-dinor and

1,2,3,4-tetranor metabolites, exert no or only weak biological activity in animal studies and are excreted primarily in the urine.

5.3 Preclinical safety data

Netarsudil

Non-clinical data with netarsudil reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity and toxicity to development. Effects in non-clinical studies were observed only at exposures considered sufficiently in excess of the maximum human exposure indicating little relevance to clinical use.

Intravenous administration of netarsudil to pregnant rats and rabbits during organogenesis did not produce adverse embryofetal effects at clinically relevant systemic exposures. In pregnant rats, 0.1 mg/kg/day showed no adverse maternal or embryofoetal effects, whereas increased post-implantation loss and reduced foetal viability was observed at 0.3 mg/kg/day and higher. In pregnant rabbits, 3 mg/kg/day showed no maternal or embryofoetal effects, whereas an increase in post-implantation loss and a decrease in foetal weight were observed at 5 mg/kg/day.

Long-term studies in animals have not been performed to evaluate the carcinogenic potential of netarsudil.

Netarsudil was not mutagenic in a bacterial mutation assay, in a mouse lymphoma assay, or in a rat micronucleus test.

Netarsudil and its active metabolite AR-13503 was found to have a possible phototoxic potential in a modified 3T3 NRU-PT *in vitro* assay, where the wavelength was extended to include UVB light.

Latanoprost

The ocular as well as systemic toxicity of latanoprost has been investigated in several animal species. Generally, latanoprost is well tolerated with a safety margin between clinical ocular dose and systemic toxicity of at least 1 000 times. High doses of latanoprost, approximately 100 times the clinical dose/kg body weight, administered intravenously to unanaesthetised monkeys have been shown to increase the respiration rate probably reflecting bronchoconstriction of short duration. In animal studies, latanoprost has not been found to have sensitising properties.

In the eye, no toxic effects have been detected with doses of up to 100 micrograms/eye/day in rabbits or monkeys (clinical dose is approximately 1.5 micrograms/eye/day). In monkeys, however, latanoprost has been shown to induce increased pigmentation of the iris. The mechanism of increased pigmentation seems to be stimulation of melanin production in melanocytes of the iris with no proliferative changes observed. The change in iris colour may be permanent.

In chronic ocular toxicity studies, administration of latanoprost 6 micrograms/eye/day has also been shown to induce increased palpebral fissure. This effect is reversible and occurs at doses above the clinical dose level. The effect has not been seen in humans.

Latanoprost was found negative in reverse mutation tests in bacteria, gene mutation in mouse lymphoma and mouse micronucleus test. Chromosome aberrations were observed *in vitro* with human lymphocytes. Similar effects were observed with prostaglandin F2α, a naturally occurring prostaglandin, and indicates that this is a class effect.

Additional mutagenicity studies on *in vitro*/*in vivo* unscheduled DNA synthesis in rats were negative and indicate that latanoprost does not have mutagenic potency. Carcinogenicity studies in mice and rats were negative.

Latanoprost has not been found to have any effect on male or female fertility in animal studies. In the embryotoxicity study in rats, no embryotoxicity was observed at intravenous doses (5, 50 and 250 micrograms/kg/day) of latanoprost. However, latanoprost induced embryolethal effects in rabbits at doses of 5 micrograms/kg/day and above.

The dose of 5 micrograms/kg/day (approximately 100 times the clinical dose) caused significant embryofoetal toxicity characterised by increased incidence of late resorption and abortion and by reduced foetal weight.

No teratogenic potential has been detected.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Benzalkonium chloride
Mannitol (E 421)
Boric acid
Sodium hydroxide (E 524) (for pH adjustment)
Water for injections

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.
Opened bottle: 4 weeks after first opening the bottle. Do not store above 25 °C.

6.4 Special precautions for storage

Store in a refrigerator (2 °C – 8 °C). Store in the original carton in order to protect from light.

For storage conditions after first opening of the medicinal product, see section 6.3.

6.5 Nature and contents of container

Roclanda is supplied (sterile) in low density polyethylene bottles (2.5 ml fill) and tips with white polypropylene screw caps and anti-tamper seals or in polypropylene bottles (2.5 ml fill) and tips with white high density polyethylene screw caps and anti-tamper seals.

Carton containing 1 or 3 bottles. Not all pack sizes may be marketed.

6.6 Special precautions for disposal

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

7. MARKETING AUTHORISATION HOLDER

Santen Oy
Niittyhaankatu 20
33720 Tampere
Finland

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/20/1502/001
EU/1/20/1502/002
EU/1/20/1502/003
EU/1/20/1502/004

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 7 January 2021
Date of latest renewal: 14 August 2025

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. MANUFACTURER 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. MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer responsible for batch release

Santen Oy
Kelloportinkatu 1
33100 Tampere
Finland

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product subject to restricted medical prescription (see Annex I: Summary of Product Characteristics, section 4.2).

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

1. NAME OF THE MEDICINAL PRODUCT

Roclanda 50 micrograms/ml + 200 micrograms/ml eye drops, solution
latanoprost + netarsudil

2. STATEMENT OF ACTIVE SUBSTANCE(S)

1 ml of solution contains 50 micrograms latanoprost and 200 micrograms netarsudil (as mesylate).

3. LIST OF EXCIPIENTS

Benzalkonium chloride, boric acid, mannitol, sodium hydroxide, water for injections. See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Eye drops, solution
1 x 2.5 ml
3 x 2.5 ml

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Ocular 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(S), IF NECESSARY

8. EXPIRY DATE

EXP
Discard 4 weeks after first opening. Once opened, do not store above 25 °C.
Open date: _____
Open date (1): _____
Open date (2): _____
Open date (3): _____

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator.
Store in the original carton in order to protect from light.

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

Santen Oy
Niittyhaankatu 20
33720 Tampere
Finland

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/20/1502/001
EU/1/20/1502/002
EU/1/20/1502/003
EU/1/20/1502/004

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Roclanda

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

BOTTLE LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Roclanda 50 micrograms/ml + 200 micrograms/ml eye drops, solution
latanoprost + netarsudil
Ocular use

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

2.5 ml

6. OTHER

B. PACKAGE LEAFLET

Package leaflet: Information for the patient

Roclanda 50 micrograms/ml + 200 micrograms/ml eye drops, solution
latanoprost + netarsudil

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

1. What Roclanda is and what it is used for

Roclanda contains the active substances latanoprost and netarsudil. Latanoprost belongs to a group of medicines known as prostaglandin analogues. Netarsudil belongs to a group of medicines called Rho kinase inhibitors. They work in different ways to reduce the amount of fluid, and so lower the pressure, inside the eye.

Roclanda is used to lower pressure in the eyes in adults who have an eye condition known as glaucoma or who have raised pressure in their eyes. If the pressure in the eye is too high, it can damage your sight.

2. What you need to know before you use Roclanda

Do not use Roclanda
- if you are allergic to latanoprost or netarsudil or any of the other ingredients of this medicine (listed in section 6).

Warnings and precautions
Talk to your doctor or pharmacist before using Roclanda if you think any of the following applies to you:
- If you suffer from dry eyes;
- If you or your child suffer from eye problems (such as eye pain, irritation or inflammation, blurred vision);
- If you have severe asthma or asthma that is not well controlled;
- If you have suffered or are currently suffering from a viral infection of the eye caused by the herpes simplex virus.
- If you wear contact lenses. You can still use Roclanda, but follow the instruction for contact lens wearers in section 3

Do not use Roclanda more than once a day, as you may experience more side effects.

Tell your doctor if you experience decreased vision or eye pain during treatment with this medicine. This might be due to a type of swelling of the clear outer layer of the eye (reticular epithelial corneal oedema). This effect has been reported following administration of this medicine to the eye in patients with certain risk factors, including previous surgery to the eye. It usually improves following discontinuation of the medicine.

Children and adolescents
Roclanda should not be used in children and adolescents under 18 years of age as it is not known if it is safe or effective in this age group.

Other medicines and Roclanda
Roclanda may interact with other medicines. Tell your doctor or pharmacist if you are using, have recently used or might use any other medicines, especially any that contain another prostaglandin analogue like latanoprost (see section 3 ‘How to use Roclanda‘).

Pregnancy and breast-feeding
If you are pregnant or breastfeeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine. Do not use Roclanda if you are pregnant or breast-feeding.

Driving and using machines
Roclanda has negligible influence on the ability to drive and use machines. You may find that your vision is blurred or abnormal just after using Roclanda. Do not drive or use machines until your vision has cleared.

Roclanda contains benzalkonium chloride
This medicine contains benzalkonium chloride which may be absorbed by soft contact lenses and change the colour of the contact lenses. You should remove contact lenses before using this medicine and not put them back before 15 minutes has passed (see section 3 ‘How to use Roclanda‘).

Benzalkonium chloride may also cause eye irritation, especially if you have dry eyes or disorders of the cornea (the clear layer at the front of the eye). If you feel abnormal eye sensation, stinging or pain in the eye after using this medicine, talk to your doctor.

3. How to use Roclanda

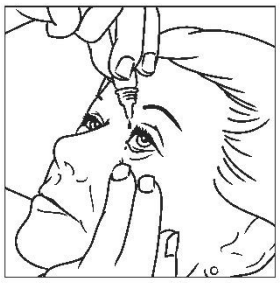
Always use this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

Only use Roclanda for your eyes (ocular use).

The recommended dose is one drop in the affected eye once a day in the evening. Use the medicine at around the same time each day. Do not use it more than once a day.

Do not use more than one drop in the affected eye once a day.

How to use



- Wash your hands before you start. Contact lenses should be removed prior to instillation of latanoprost + netarsudil (see section 2 ‘Warning and precautions’).
- Do not touch the dropper tip with your fingers when opening or closing the bottle. It could contaminate the eye drops.
- Twist off the bottle cap, and lie the cap on a clean surface on its side. Continue to hold the bottle, ensuring that the tip doesn’t come into contact with anything.
- Hold the bottle, pointing down, between your thumb and fingers.
- Tilt your head back.
- Pull down your lower eyelid with a clean finger to form a ‘pocket’ between the eyelid and your eye. The drop will go in here.
- Bring the dropper tip close to the eye. Do this in front of a mirror if it helps.
- Do not touch your eye, eyelid, surrounding areas or other surfaces with the dropper tip. It could contaminate the eye drops.
- Gently squeeze the bottle to release one drop of Roclanda into your eye.
- Only put one drop into your eye each time. If a drop misses your eye, try again.
- Press a finger against the corner of the eye by the nose. Hold for 1 minute whilst keeping the eye closed.
- **If you need to use the drops in both eyes**, repeat the steps for your other eye while you have the bottle open.
- Put back the bottle cap to close the bottle.
- Put the bottle back into the carton to protect the drops from light until you need to use the drops again.

If you are using other eye drops, wait at least five minutes after using them and then use Roclanda last due to netarsudil’s ability to widen blood vessels. If you are using an eye ointment, it should be used last.

If you use more Roclanda than you should
Rinse your eye with warm water. Do not put in any more drops until it is time for your next regular dose.

If you forget to use Roclanda
Continue with the next dose as planned. Do not use a double dose to make up for a forgotten dose.

If you stop using Roclanda
Do not stop using Roclanda without first speaking to your doctor. If you stop using Roclanda the pressure in your eye will not be controlled which could lead to loss of sight.

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. You can usually carry on taking the drops, unless the effects are serious. If you are worried, talk to your doctor or pharmacist. Do not stop using these eye drops without speaking to your doctor.

The following side effects have been observed with Roclanda and other medicines containing latanoprost and netarsudil alone:

- **Very common (may affect more than 1 in 10 people)**
  - *Effects in the eye:*
    - Eye redness; fine deposits on the front of the eye (corneal verticillata)
    - Pain where the drops have been put in
    - A gradual increase in the amount of brown pigment in the coloured part of the eye (the iris) leading to altered eye colour
    - A gradual increase in the colour (darkening), length, thickness and number of your eye lashes
- **Common (may affect up to 1 in 10 people)**
  - *Effects in the eye:*
    - General eye redness shortly after drops are put in; spots or patches of eye redness
    - Infection or inflammation of the eye; conjunctivitis (eye inflammation or prominent blood vessels) caused by an allergic reaction; dryness of the eye or small breaks in the film of liquid on the surface of the eye (punctate keratitis)
    - Eye discharge; watery eyes
    - Itchy eyelids; swelling around the eye; eyelid crusting
    - Clouding of the eye and slight decrease in vision; blurred vision
    - Eye pain; feeling of grittiness or having something in the eye
  - *General side effects*
    - Redness or itching of the skin on your face
- **Uncommon (may affect up to 1 in 100 people)**
  - *Effects in the eye:*
    - Increased fluid pressure inside the eye
    - Inflammation of the coloured part of the eye (the iris); bulging of iris
    - Increased wrinkling of the clear layer over the eye where it meets with the lower eyelid (conjunctivochalasis); small colored spots on the eye surface; shiny/glassy eyes; tiredness; numbness or burning in the eye; increased sensitivity to light
    - Eye allergy
    - Blindness; double or halo vision
    - Blocked tear duct; eye dryness caused by inflammation of the glands of the eyelids
    - Abnormal turning outward of the lower eyelid; loss of eyelashes (madarosis); discoloration of eyelid skin
    - Eye disease related to diabetes (diabetic retinopathy)
  - *Side effects in other parts of the body*
    - Blocked nose; nosebleed; nasal discomfort and pain
    - Headache; dizziness; feeling sick (nausea, vomiting)
    - Redness or itching of the skin; dry skin; thickening of the skin; picking at your skin
    - Muscle pain or spasm or weakness; joint pain; jaw pain; inflammation of the cartilage
    - Chest pain (angina); awareness of heart beat (palpitations)
    - Asthma; shortness of breath (dyspnoea)
- **Rare (may affect up to 1 in 1 000 people)**
  - *Effects in the eye:*
    - Swelling or scratching with damage to the surface of the eye; swelling around the eye (periorbital oedema); scarring of the surface of the eye
    - Eyelashes growing in the wrong direction or an extra row of eyelashes
    - Fluid filled area within the coloured part of the eye (iris cyst)
    - Skin reactions on the eyelids; darkening of the skin of the eyelids
    - Viral infection of the eye caused by herpes simplex virus (HSV)

- *Side effects in other parts of the body*
  - Worsening of asthma
  - Severe itching of the skin
- **Very rare (may affect up to 1 in 10 000 people)**
  - *Effects in the eye:*
    - Sunken eye appearance (eye sulcus deepening).
  - *Side effects in other parts of the body*
    - Worsening of angina in patients who also have heart disease
- **Not known (cannot be estimated from the available data)**
  - *Effects in the eye:*
    - Swelling of the clear outer layer of the eye (reticular epithelial corneal oedema)

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 affects you can help provide more information on the safety of this medicine.

5. How to store Roclanda

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 carton and bottle label after "EXP". The expiry date refers to the last day of that month.

Unopened bottle: Store in a refrigerator (2 °C – 8 °C).
After opening the bottle: Do not store above 25 °C.

Store in the original carton in order to protect from light.

Do not use the bottle 4 weeks after first opening to prevent infections and use a new bottle.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Roclanda contains
- The active substances are latanoprost and netarsudil. Each ml of solution contains 50 micrograms latanoprost and 200 micrograms netarsudil (as mesylate).
- The other excipients are benzalkonium chloride (see section 2 under 'Roclanda contains benzalkonium chloride'), mannitol (E 421), boric acid, sodium hydroxide (E 524) (for pH adjustment) and water for injections.

What Roclanda looks like and contents of the pack
Roclanda 50 micrograms/ml + 200 micrograms/ml eye drops, solution (eye drops) is a clear, liquid eye drop solution in a plastic bottle. Each bottle contains 2.5 ml of the medicine and each pack contains 1 or 3 bottles with a screw-cap. Not all pack sizes may be marketed.

Marketing Authorisation Holder
Santen Oy
Niittyhaankatu 20, 33720 Tampere, Finland

Manufacturer
Santen Oy,
Kelloportinkatu 1, 33100 Tampere, Finland

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

België/Belgique/Belgien
Santen Oy
Tél/Tel: +32 (0) 24019172

България
Santen Oy
Тел.: +40 21 528 0290

Česká republika
Santen Oy
Tel: +358 (0) 3 284 8111

Danmark
Santen Oy
Tlf.: +45 898 713 35

Deutschland
Santen GmbH
Tel: +49 (0) 3030809610

Eesti
Santen Oy
Tel: +372 5067559

Ελλάδα
Santen Oy
Τηλ: + 358 (0) 3 284 8111

España
Santen Pharmaceutical Spain S.L.
Tel: + 34 914 142 485

France
Santen S.A.S.
Tél: +33 (0) 1 70 75 26 84

Hrvatska
Santen Oy
Tel: +358 (0) 3 284 8111

Ireland
Santen Oy
Tel: +353 (0) 16950008

Ísland
Santen Oy
Sími: +358 (0) 3 284 8111

Italia
Santen Italy S.r.l.

Lietuva
Santen Oy
Tel: +370 37 366628

Luxembourg/Luxemburg
Santen Oy
Tél/Tel: +352 (0) 27862006

Magyarország
Santen Oy
Tel: +358 (0) 3 284 8111

Malta
Santen Oy
Tel: +358 (0) 3 284 8111

Nederland
Santen Oy
Tel: +31 (0) 207139206

Norge
Santen Oy
Tlf: +47 21939612

Österreich
Santen Oy
Tel: +43 (0) 720116199

Polska
Santen Oy
Tel.: +48(0) 221042096

Portugal
Santen Oy
Tel: +351 308 805 912

România
Santen Oy
Tel: +358 (0) 3 284 8111

Slovenija
Santen Oy
Tel: +358 (0) 3 284 8111

Slovenská republika
Santen Oy
Tel: +358 (0) 3 284 8111

Suomi/Finland
Santen Oy

Tel: +39 0236009983

Puh/Tel: +358 (0) 974790211

Κύπρος
Santen Oy
Τηλ: +358 (0) 3 284 8111

Sverige
Santen Oy
Tel: +46 (0) 850598833

Latvija
Santen Oy
Tel: +371 677 917 80

This leaflet was last revised in

Other sources of information

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