ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 for how to report adverse reactions.

1. NAME OF THE MEDICINAL PRODUCT

Anzupgo 20 mg/g cream

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each gram of cream contains 20 mg of delgocitinib.

Excipients with known effect

Each gram of cream contains 10 mg of benzyl alcohol (E 1519), 0.2 mg of butylhydroxyanisole (E 320), and 72 mg of cetostearyl alcohol.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Cream

White to slightly brown cream

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Anzupgo is indicated for the treatment of moderate to severe chronic hand eczema (CHE) in adults for whom topical corticosteroids are inadequate or inappropriate (see section 5.1).

4.2 Posology and method of administration

Anzupgo should be initiated and supervised by physicians with experience in the diagnosis and treatment of chronic hand eczema.

Posology

A thin layer of Anzupgo should be applied twice daily to the affected skin of the hands and wrists until the skin is clear or almost clear (see section 5.1). It is recommended to apply the cream at regular intervals, approximately 12 hours apart.

In the event of recurrence of the signs and symptoms of CHE (flares), twice daily treatment of the affected areas should be re-initiated as needed.

Treatment should be discontinued if no improvement is seen after 12 weeks of continuous treatment.

Missed dose

If an application is missed, the cream should be applied as soon as possible. Thereafter, applications should be resumed at the regular scheduled time.

Special populations

Elderly patients
No dose adjustment is recommended for elderly patients.

Hepatic and renal impairment
No studies with Anzupgo have been performed in patients with severe hepatic or renal impairment. However, dose adjustment is not recommended due to the minimal systemic exposure of topically applied delgocitinib (see section 5.2).

Paediatric population
The safety and efficacy of Anzupgo in children and adolescents below 18 years of age has not been established. No data are available.

Method of administration

Anzupgo is for cutaneous use only. A thin layer of Anzupgo should be applied to clean and dry skin of the affected areas of the hands and wrists. Patients should avoid applying other topical products immediately before and after application of Anzupgo (see section 4.5). Co-application with emollients within 2 hours before and after application of delgocitinib has not been studied.

If someone else applies the cream to the patient, they should be instructed to wash their hands after application.

Contact with eyes, mouth, or other mucous membranes should be avoided. If contact with mucous membranes occurs, rinse thoroughly with water.

4.3 Contraindications

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

4.4 Special warnings and precautions for use

Non-melanoma skin cancer

Non-melanoma skin cancer (NMSC), predominantly basal cell carcinoma, has been reported in patients treated with topical JAK inhibitors. Periodic skin examination of the application site is recommended for all patients, particularly those with risk factors for skin cancer.

Excipients with known effect

Benzyl alcohol
This medicinal product contains 10 mg benzyl alcohol (E 1519) in each gram of cream.
Benzyl alcohol may cause allergic reactions or mild local irritation.

Butylhydroxyanisole
Butylhydroxyanisole (E 320) may cause local skin reactions (e.g. contact dermatitis), or irritation to the eyes and mucous membranes.

Cetostearyl alcohol
Cetostearyl alcohol may cause local skin reactions (e.g. contact dermatitis).

4.5 Interaction with other medicinal products and other forms of interaction

No clinical interaction studies have been performed with topically or systemically administered delgocitinib (see section 5.2 for *in vitro* interaction studies). Given the limited metabolism of delgocitinib, application to a limited body surface area (hands and wrists), and minimal systemic

exposure of topically applied delgocitinib, there is a low potential for interaction with systemic treatments.

Delgocitinib has not been evaluated in combination with other topical medicinal products and co-application on the same skin area is not recommended.

4.6 Fertility, pregnancy and lactation

Pregnancy

There are no or a limited amount of data (less than 300 pregnancy outcomes) from the use of delgocitinib in pregnant women.

Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity (see section 5.3).

As a precautionary measure, it is preferable to avoid the use of Anzupgo during pregnancy.

Breast-feeding

No effects on the breastfed newborn/infant are anticipated since the systemic exposure of the breast-feeding woman to delgocitinib is negligible (see section 5.3).

Anzupgo can be used during breast-feeding.

When Anzupgo is used during breast-feeding, care should be taken to avoid direct contact with the nipple or surrounding area after applying the cream to the hands and/or wrists.

As a precautionary measure, care should be taken to avoid direct skin contact when taking care of an infant immediately after applying Anzupgo to the hands and/or wrists.

Fertility

No human data on the effect of delgocitinib on fertility are available.

Based on findings in female rats, oral administration of delgocitinib resulted in reduced fertility at exposures considered sufficiently in excess of the human exposure (see section 5.3).

Animal studies did not indicate effects with respect to fertility in males.

4.7 Effects on ability to drive and use machines

Anzupgo has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Summary of the safety profile

The most common adverse reactions were application site reactions (1.0%).

Tabulated list of adverse reactions

Table 1 lists the adverse reactions that were observed in clinical studies. The adverse reactions are presented by MedDRA system organ class and frequency, using the following categories: 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).

Table 1 Adverse reactions

System Organ Class	Frequency	Adverse reaction
General disorders and administration site conditions	Common	Application site reactions*

*see Description of selected adverse reactions

Description of selected adverse reactions

Application site reactions
In the pool of three vehicle-controlled clinical studies through 16 weeks, 9 application site reactions (including application site pain, application site paraesthesia, application site pruritus, and application site erythema) were reported in 1.0% of patients treated with delgocitinib cream. 8 application site reactions were mild in severity and 1 was moderate. 7 of 9 occurred within the first week of treatment. No application site reactions resulted in treatment interruption, and the median time to resolution was 3 days.

The event rate of application site reactions in the long-term extension study (0.56 events per 100 patient years of observation) was lower than in the 16-week vehicle-controlled clinical studies (4.11 events per 100 patient years of observation).

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

No systemic signs of overdose are expected following topical application of Anzupgo due to the minimal systemic absorption of delgocitinib. If too much cream has been applied, the excess can be wiped off.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Other dermatological preparations, agents for dermatitis, excluding corticosteroids, ATC code: D11AH11

Mechanism of action

Delgocitinib is a pan Janus kinase (JAK) inhibitor that targets the activity of all four members of the JAK family of enzymes consisting of JAK1, JAK2, JAK3, and tyrosine kinase 2 (TYK2) in a concentration dependent manner.

In human cells, inhibition of the JAK-STAT pathway by delgocitinib attenuates the signalling of several pro-inflammatory cytokines (including interleukin (IL)-2, IL-4, IL-6, IL-13, IL-21, IL-23, Granulocyte-Macrophage-Colony-Stimulating Factor (GM-CSF), and Interferon (IFN)-α) downregulating the immune and inflammatory responses in cells of relevance to CHE pathology.

Pharmacodynamic effects

In a thorough QT study in healthy subjects, there was no indication of a QTc prolonging effect of orally administered delgocitinib at single doses up to 12 mg (approximately 200 times the human

exposure following topical application, based on C_{max}). Therefore, Anzupgo is not expected to affect cardiac repolarisation under conditions of clinical use.

Dermal safety studies

Clinical studies in healthy subjects demonstrated that delgocitinib cream did not cause phototoxic skin reactions or photoallergic skin reactions.

Clinical efficacy and safety

The safety and efficacy of delgocitinib cream were evaluated in two pivotal randomised, double-blind, vehicle-controlled studies of similar design (DELTA 1 and DELTA 2). CHE was defined as hand eczema that has persisted for more than 3 months or returned twice or more within the last 12 months. The studies included 960 patients 18 years of age and older with moderate to severe CHE as defined by an Investigator's Global Assessment for chronic hand eczema (IGA-CHE) score of 3 or 4 (moderate or severe) (see Table 2) and required a Hand Eczema Symptom Diary (HESD) itch score of ≥ 4 points at baseline. Eligible patients had a previous inadequate response to topical corticosteroids or were those in which topical corticosteroids are not advisable (e.g. due to important side effects or safety risks).

Table 2 Investigator's Global Assessment for chronic hand eczema (IGA-CHE)

IGA-CHE severity	**IGA-CHE score**	**Sign and intensity**
Clear	0	No signs of erythema, scaling, hyperkeratosis/lichenification, vesiculation, oedema or fissures
Almost clear	1	Barely perceptible erythema No signs of scaling, hyperkeratosis/lichenification, vesiculation, oedema or fissures
Mild	2	At least one: • Slight but definite erythema (pink) • Slight but definite scaling (mostly fine scales) • Slight but definite hyperkeratosis/lichenification and at least one: • Scattered vesicles, without erosion • Barely palpable oedema • Superficial fissures
Moderate	3	At least one: • Clearly perceptible erythema (dull red) • Clearly perceptible scaling (coarse scales) • Clearly perceptible hyperkeratosis/lichenification and at least one: • Clustered vesicles, without visible erosions • Definite oedema • Definite fissures
Severe	4	At least one: • Marked erythema (deep or bright red) • Marked and thick scaling • Marked hyperkeratosis/lichenification and at least one: • High density of vesicles with erosions • Marked oedema • One or more deep fissures

In DELTA 1 and DELTA 2, patients applied either delgocitinib 20 mg/g cream or vehicle cream twice daily to affected areas on the hands and wrists for 16 weeks. All patients who completed the two pivotal studies were eligible to enrol into the long-term extension study DELTA 3.

Endpoints
In DELTA 1 and DELTA 2, the primary endpoint was the proportion of patients achieving IGA-CHE treatment success (IGA-CHE TS), defined as an IGA-CHE score of 0 (clear) or 1 (almost clear: barely perceptible erythema only) with at least a 2-step improvement from baseline to Week 16. The IGA-CHE instrument rates the severity of the subject's global disease and is based on a 5-point scale ranging from 0 (clear) to 4 (severe).

Additional efficacy outcomes included the Hand Eczema Severity Index (HECSI) and the HESD at various timepoints. The HECSI rates the severity of six clinical signs (erythema, infiltration/papulation, vesicles, fissures, scaling, and oedema) and the extent of the lesions on each of the five hand regions (fingertips, fingers, palm of hands, back of hands, and wrists). The HESD is a daily 6-item patient-reported outcome (PRO) instrument designed to assess the worst severity of signs and symptoms of CHE (itch, pain, cracking, redness, dryness, and flaking) using an 11-point numeric rating scale.

Baseline characteristics
Across all treatment groups in DELTA 1 and DELTA 2, the mean age was 44.1 years, 7.6% of patients were 65 years of age or older, 64.4% were female, 90.4% were White, 3.5% were Asian, and 0.7% were Black. The frequency of CHE by main subtype was 35.9% atopic hand eczema, 21.5% hyperkeratotic eczema, 19.6% irritant contact dermatitis, 13.9% allergic contact dermatitis, 9.1% vesicular hand eczema (pompholyx), and 0.1% contact urticaria/protein contact dermatitis. In DELTA 1 and DELTA 2, 71.6% of patients had a baseline IGA-CHE score of 3 (moderate CHE), and 28.4% of patients had a baseline IGA-CHE score of 4 (severe CHE). The mean baseline Dermatology Life Quality Index (DLQI) score was 12.5, HECSI score was 71.6, and HESD score was 7.1. The mean HESD itch and pain scores were 7.1 and 6.7, respectively.

Clinical response

DELTA 1 and DELTA 2
In DELTA 1 and DELTA 2, a statistically significantly greater proportion of patients randomised to delgocitinib cream achieved the primary endpoint of IGA-CHE TS compared to vehicle at Week 16. The results for the primary and most relevant multiplicity-controlled secondary endpoints are presented in Table 3. Figure 1 shows the proportion of patients who achieved HESD itch ≥ 4-point improvement, and HESD pain ≥ 4-point improvement over time in DELTA 1 and DELTA 2.

Table 3 Efficacy results of delgocitinib cream at Week 16 in DELTA 1 and DELTA 2

	DELTA 1		DELTA 2	
	Delgocitinib (N=325)	**Vehicle (N=162)**	**Delgocitinib (N=313)**	**Vehicle (N=159)**
IGA-CHE TS, % responders[a]	19.7[#]	9.9	29.1[§]	6.9
HECSI-90, % responders[a, b]	29.5[§]	12.3	31.0[§]	8.8
HECSI-75, % responders[a, c]	49.2[§]	23.5	49.5[§]	18.2
HECSI, LS mean % change from baseline (± SE)[d]	-56.5[§] (± 3.4)	-21.2 (± 4.8)	-58.9[§] (± 3.2)	-13.4 (± 4.5)
HESD itch ≥ 4-point improvement, % responders[a, e]	47.1[§] (152/323)	23.0 (37/161)	47.2[§] (146/309)	19.9 (31/156)
HESD pain ≥ 4-point improvement, % responders[a, e]	49.1[§] (143/291)	27.5 (41/149)	48.6[§] (143/294)	22.7 (32/141)
HESD ≥ 4-point improvement, % responders[a, e]	47.2[§] (146/309)	24.4 (38/156)	44.5[§] (137/308)	20.9 (32/153)

#p < 0.01, §p < 0.001

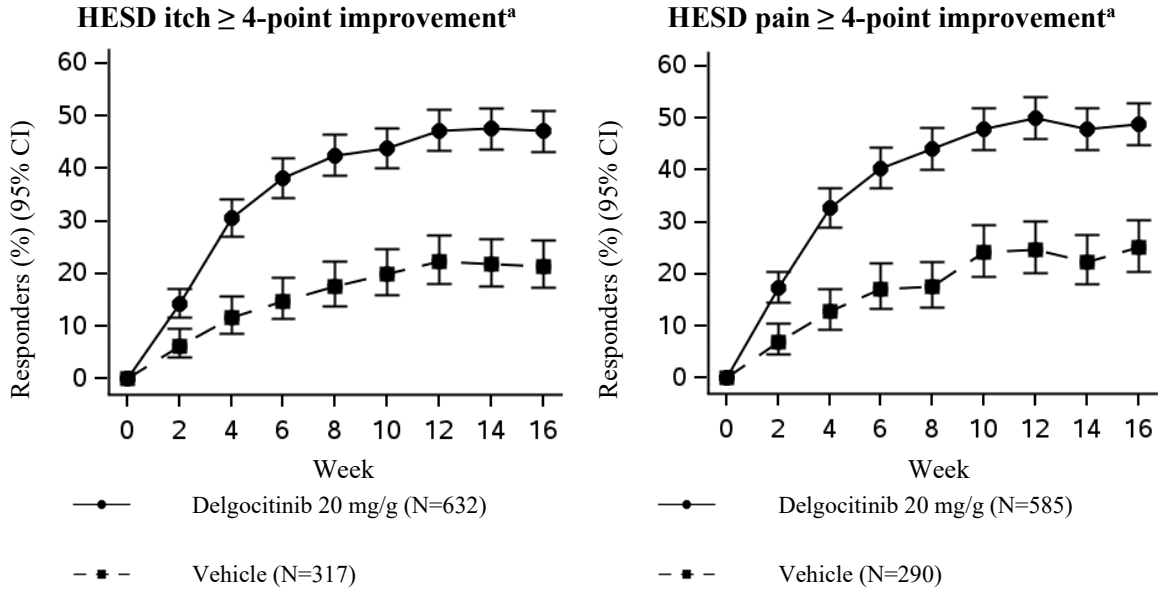
All p-values were statistically significant versus vehicle with adjustment for multiplicity.

Abbreviations: LS=least squares; N=number of patients in the full analysis set (all patients randomised and dosed); SE=standard error

a. Data after initiation of rescue treatment, permanent discontinuation of treatment, or missing data were considered non-response.
b. HECSI-90 responders were patients with ≥ 90% improvement in HECSI from baseline.
c. HECSI-75 responders were patients with ≥ 75% improvement in HECSI from baseline.
d. Data after initiation of rescue treatment, permanent discontinuation of treatment, or missing data were considered non-response by using worst observation carried forward.
e. Based on the number of patients whose baseline value was ≥ 4 (scale from 0-10).

In both DELTA 1 and DELTA 2, a statistically significantly greater proportion of patients treated with delgocitinib cream achieved IGA-CHE TS and a ≥ 4-point improvement in HESD as early as Week 4 compared to vehicle. A statistically significantly greater proportion of patients treated with delgocitinib cream achieved HECSI-75 at Week 8 compared to vehicle.

Figure 1 Proportion of patients who achieved HESD itch ≥ 4-point improvement and HESD pain ≥ 4-point improvement over time – pooled data from DELTA 1 and DELTA 2



CI = Confidence Interval

a. Based on the number of patients whose baseline value was ≥ 4 (scale from 0-10).

Additional quality of life/patient-reported outcomes

In both DELTA 1 and DELTA 2, patients treated with delgocitinib cream showed a statistically significantly greater improvement from baseline to Week 16 compared to vehicle in the Hand Eczema Impact Scale (HEIS) (see Table 4). HEIS is an instrument used for assessing the patient's perceived impact on their daily activities (use of soaps/cleaning products, housework involving hands getting wet, washing themselves, embarrassment, frustration, sleep, work, and the ability to hold or grip objects). 9 items are scored on a 5-point scale where 0='not at all' and 4='extremely', and the HEIS score is then calculated as the average of the 9 items.

Across DELTA 1 and DELTA 2, statistically significantly greater improvements in health-related quality of life, as measured by the DLQI were observed in delgocitinib patients compared to vehicle at Week 16 (see Table 4).

Table 4 Quality of life/patient-reported outcomes results of delgocitinib cream at Week 16 in DELTA 1 and DELTA 2

	DELTA 1		DELTA 2	
	Delgocitinib (N=325)	**Vehicle (N=162)**	**Delgocitinib (N=313)**	**Vehicle (N=159)**
HEIS, LS mean change from baseline (± SE)[a]	-1.46[§] (± 0.05)	-0.82 (± 0.08)	-1.45[§] (± 0.06)	-0.64 (± 0.08)
HEIS PDAL, LS mean change from baseline (± SE)[a, b]	-1.46[§] (± 0.06)	-0.86 (± 0.08)	-1.48[§] (± 0.06)	-0.66 (± 0.08)
DLQI ≥ 4-point improvement, % responders[c, d]	74.4[§] (227/305)	50.0 (74/148)	72.2[§] (216/299)	45.8 (70/153)

[§] $p < 0.001$

All p-values were statistically significant versus vehicle with adjustment for multiplicity.

Abbreviations: LS=least squares; N=number of patients in the full analysis set (all patients randomised and dosed); PDAL=proximal daily activity limitations; SE=standard error

a. Data after initiation of rescue treatment, permanent discontinuation of treatment, or missing data were considered non-response by using worst observation carried forward.
b. HEIS PDAL assesses the patient's ability to use soaps/cleaning products, to do housework, and to wash themselves. The HEIS PDAL score is calculated as the average of the 3 items.
c. Data after initiation of rescue treatment, permanent discontinuation of treatment, or missing data were considered non-response.
d. Based on the number of patients whose baseline value was ≥ 4.

Extension study (DELTA 3)

Patients who completed either DELTA 1 or DELTA 2 were eligible to enrol in a 36-week open-label extension study (DELTA 3). In DELTA 3, the long-term safety and efficacy of as-needed delgocitinib treatment was evaluated in 801 patients. Patients started application of delgocitinib cream twice daily to affected areas whenever the IGA-CHE score was ≥ 2 (mild or worse) and stopped treatment when an IGA-CHE score of 0 or 1 (clear or almost clear) was achieved. Patients entering DELTA 3 with an IGA-CHE score of 0 or 1 remained off treatment until loss of response (IGA-CHE score ≥ 2).

The proportions of patients achieving IGA-CHE 0 or 1, HECSI-75, HECSI-90, HESD itch ≥ 4-point improvement, and HESD pain ≥ 4-point improvement after the initial 16-week treatment period of delgocitinib cream were maintained through Week 52 with as-needed treatment. Among the 560 patients randomised to delgocitinib cream treatment in the pivotal studies (DELTA 1 and DELTA 2) enrolled in DELTA 3, the mean number of treatment periods was 1.5 (range 0 to 6), the mean treatment period duration was 123 days, and the mean cumulative number of days in response (days with an IGA-CHE score of 0 or 1 within the 36-week treatment period) was 46. The mean cumulative number of days in response was 111 among those patients who achieved IGA-CHE TS at Week 16 in the pivotal studies.

Of the patients randomised to delgocitinib cream in the pivotal studies who achieved IGA-CHE TS at Week 16, the median duration of response while off treatment was 4 weeks with 28.3% maintaining response for at least 8 weeks. The median time to regain an IGA-CHE score of 0 or 1 following re-initiation of treatment was 8 weeks. Among patients who did not achieve an IGA-CHE TS at Week 16 of delgocitinib treatment in the pivotal studies, 48.1% achieved IGA-CHE 0 or 1 with continued delgocitinib treatment in DELTA 3.

Phase 3 active comparator study versus alitretinoin (DELTA FORCE)

The efficacy and safety of delgocitinib cream compared to alitretinoin was evaluated in a randomised, assessor-blinded, 24-week study with 513 patients 18 years of age and older with severe CHE as defined by an IGA-CHE score of 4. Eligible patients had a previous inadequate response to topical corticosteroids or were those in which topical corticosteroids are not advisable. The patients were randomised to either delgocitinib 20 mg/g cream twice-daily treatment for 16 weeks or alitretinoin 30 mg capsules once-daily treatment (with an option to reduce to 10 mg once daily) for 12 weeks. Treatment could continue up to 24 weeks. Permanent discontinuation of treatment (35.9% for alitretinoin vs. 13.4% for delgocitinib) and use of rescue medications (8.1% for alitretinoin vs. 4.7% for delgocitinib) were more frequent for patients treated with alitretinoin compared to delgocitinib.

Statistically significantly greater improvements for the primary endpoint, change in HECSI score from baseline to Week 12, was achieved for delgocitinib cream compared to alitretinoin. Statistically significantly greater improvements were also achieved for delgocitinib cream for HECSI-90 and IGA-CHE TS. The results for the primary and the most relevant secondary endpoints are presented in Table 5.

Table 5 Efficacy results at Week 12 from DELTA FORCE – delgocitinib cream versus alitretinoin

	DELTA FORCE	
	Delgocitinib (N=250)	**Alitretinoin (N=253)**
HECSI, LS mean change from baseline (± SE)[a]	-67.6[§] (± 3.37)	-51.5 (± 3.36)
HECSI-90, % responders[b, c]	38.6[#] (96/249)	26.0 (65/250)
HECSI-75, % responders[b, d, e]	55.4[*] (138/249)	46.0 (115/250)
IGA-CHE TS, % responders[b]	27.2[#]	16.6

*p < 0.05, #p < 0.01, §p < 0.001

All p-values were statistically significant versus alitretinoin with adjustment for multiplicity, except HECSI-75 % responders, which was not a multiplicity adjusted endpoint.

Abbreviations: LS=least squares; N=number of patients in the full analysis set; SE=standard error

a. Data after initiation of rescue treatment, permanent discontinuation of treatment, or missing data were considered non-response by using worst observation carried forward.

b. Data after initiation of rescue treatment, permanent discontinuation of treatment, or missing data were considered non-response.

c. HECSI-90 responders were patients with ≥ 90% improvement in HECSI from baseline.

d. HECSI-75 responders were patients with ≥ 75% improvement in HECSI from baseline.

e. HECSI-75 % responders were not a multiplicity adjusted endpoint.

Greater improvements for delgocitinib cream measured by the mean change in HECSI score compared to alitretinoin, were observed at Week 1 and maintained through to Week 24.

Paediatric population

The European Medicines Agency has deferred the obligation to submit the results of studies with delgocitinib in one or more subset of the paediatric population for the treatment of chronic hand eczema (see section 4.2 for information on paediatric use).

5.2 Pharmacokinetic properties

Absorption

The pharmacokinetics of delgocitinib cream were evaluated in a study involving 15 adult patients 22 to 69 years of age with moderate to severe CHE. Patients applied on average 0.87 g of delgocitinib 20 mg/g cream to the affected areas of the hands and wrists twice a day for 8 days.

The geometric mean (GSD) maximum plasma concentration (C_{max}) and area under the concentration-curve from time 0 to 12 hours (AUC_{0-12}) on Day 8 was 0.46 ng/mL (1.74) and 3.7 ng*h/mL (1.74), respectively. Steady state was reached by Day 8. The systemic exposure (AUC and C_{max}) between Day 1 and Day 8 were similar.

Following twice daily application of delgocitinib 20 mg/g cream in DELTA 2, the geometric mean plasma concentration observed 2-6 hours after application at Day 113 was 48% lower than that at Day 8 (0.11 ng/mL and 0.21 ng/mL, respectively).

The relative bioavailability of delgocitinib following topical application is approximately 0.6% compared to administration via oral tablets.

Distribution

Based on an *in vitro* study, plasma protein binding of delgocitinib is 22 to 29%.

Biotransformation

As delgocitinib does not undergo extensive metabolism, the main plasma component is unchanged delgocitinib. Following oral administration, four metabolites (formed via oxidation and glucuronide conjugation) were detected at < 2% of the average unchanged delgocitinib plasma concentrations. The limited metabolism of delgocitinib occurs primarily though CYP3A4/5 and to a lesser extent by CYP1A1, CYP2C19, and CYP2D6.

In vitro interaction studies

Based on *in vitro* data, delgocitinib does not inhibit or induce cytochrome P450 enzymes or inhibit transporter systems such as organic anion transporters (OAT), organic anion transporting polypeptides (OATP), organic cation transporters (OCT), P-glycoprotein (P-gp), breast cancer resistance protein (BCRP), or multidrug and toxin extrusion proteins (MATE) at clinically relevant concentrations.

Delgocitinib is a substrate of P-glycoprotein (P-gp) and a weak substrate of human organic cation transporter 2 (OTC2) and human organic anion transporter 3 (OAT3).

Elimination

Delgocitinib is primarily eliminated by renal excretion as approximately 70-80% of the total dose after oral administration was found unchanged in the urine.

Following repeated topical application of delgocitinib cream, the average half-life of delgocitinib was estimated to be 20.3 hours.

Special populations

Hepatic impairment
No formal studies of delgocitinib cream in patients with hepatic impairment have been conducted.

Due to the minimal systemic exposure of topically applied delgocitinib and limited metabolism of delgocitinib, changes in hepatic function are unlikely to have any effect on the elimination of delgocitinib (see section 4.2).

Renal impairment
Pharmacokinetic parameters of delgocitinib were analysed in 96 patients with mild or moderate renal impairment (eGFR 30 to 89 mL/min/1.73 m2) in DELTA 2. There were no clinically relevant differences in the pharmacokinetics observed in patients with mild or moderate renal impairment compared to the overall study population. Renal function impairment is unlikely to result in clinically important changes in exposure to delgocitinib due to the minimal systemic exposure following topical administration (see section 4.2).

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, genotoxicity, phototoxicity, local tolerability, skin sensitisation, and juvenile toxicity. Effects in repeat dose toxicity studies were observed only at exposures considered sufficiently in excess of the maximum human exposure following topical application.

Carcinogenicity

In a 2-year dermal carcinogenicity study in mice, no local or systemic drug-related neoplastic findings were observed (at exposures up to approximately 600 times the human exposure based on AUC).

Fertility and early embryonic development

Orally administered delgocitinib did not result in effects on fertility at any dose level evaluated in male rats (exposures approximately 1 700 times the human exposure). In female rats, orally administered delgocitinib resulted in effects on female fertility (lower fertility index, fewer corpora lutea, and fewer implantations) at exposures approximately 5 800 times the human exposure. Post-implantation losses and a decrease in the number of live embryos were observed at exposures approximately 432 and 1 000 times the human exposure, respectively.

Embryo-foetal development

Orally administered delgocitinib did not result in adverse effects to the foetus in rats or rabbits at exposures approximately 120 and 194 times the human exposure, respectively. Teratogenic effects were not observed at any dose studied in rats or rabbits (exposures approximately 1 400 and 992 times the human exposure, respectively).

In rats, decreases in foetal weight and skeletal variations were observed at exposures 512 times the human exposure and a tendency toward an increase in post-implantation loss was observed at exposures approximately 1 400 times the human exposure. In rabbits, an increase in post-implantation loss, a reduced number of live foetuses, and a tendency toward a decrease in foetal weights were observed at exposures approximately 992 times the human exposure.

No effects during pregnancy are anticipated, since systemic exposure to delgocitinib is negligible. As a precautionary measure, it is preferable to avoid the use of delgocitinib during pregnancy (see section 4.6).

Pre-and postnatal development

Orally administered delgocitinib in rats resulted in decreased foetal viability and reduced pup weights during the early postnatal period at exposures > 2 000 times the human exposure. There was no effect on behavioural and learning assessments, sexual maturation, or reproductive performance of the offspring at any dose studied.

Following oral administration to lactating rats, delgocitinib was secreted in milk at concentrations approximately 3-fold those in the plasma.

No effects on the breastfed newborn/infant are anticipated since the systemic exposure in the breast-feeding woman to delgocitinib is negligible. Delgocitinib can therefore be used during breast-feeding (see section 4.6).

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Benzyl alcohol (E 1519)
Butylhydroxyanisole (E 320)
Cetostearyl alcohol
Citric acid monohydrate (E 330)
Disodium edetate
Hydrochloric acid (E 507) (for pH-adjustment)
Liquid paraffin
Macrogol cetostearyl ether
Purified water

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years

After first opening: 1 year

6.4 Special precautions for storage

Do not freeze.

6.5 Nature and contents of container

Laminate tube with an aluminium barrier layer and an inner layer of low-density polyethylene fitted with a polypropylene flip-top cap.

Package sizes:
- 1 tube of 15 g or 60 g
- Multipacks containing 3 tubes (2 tubes of 15 g and 1 tube of 60 g)

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

LEO Pharma A/S
Industriparken 55
DK-2750 Ballerup
Denmark

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/24/1851/001
EU/1/24/1851/002
EU/1/24/1851/003

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 19 September 2024

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

LEO Laboratories Ltd.
285 Cashel Road
Crumlin, Dublin 12
Ireland

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.

The marketing authorisation holder (MAH) shall submit the first PSUR for this product within 6 months following authorisation.

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

Anzupgo 20 mg/g cream
delgocitinib

2. STATEMENT OF ACTIVE SUBSTANCE(S)

1 g of cream contains 20 mg delgocitinib.

3. LIST OF EXCIPIENTS

Excipients: benzyl alcohol (E 1519), butylhydroxyanisole (E 320), cetostearyl alcohol, citric acid monohydrate (E 330), disodium edetate, hydrochloric acid (E 507), liquid paraffin, macrogol cetostearyl ether, purified water.

4. PHARMACEUTICAL FORM AND CONTENTS

Cream

1 tube (15 g)
1 tube (60 g)

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Cutaneous use

Read the package leaflet before 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

9. SPECIAL STORAGE CONDITIONS

Do not freeze.

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

LEO Pharma A/S
Industriparken 55
DK-2750 Ballerup
Denmark

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/24/1851/001 1 tube (15 g)
EU/1/24/1851/002 1 tube (60 g)

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Anzupgo 20 mg/g

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 FOR MULTIPACK (INCLUDING BLUE BOX)

1. NAME OF THE MEDICINAL PRODUCT

Anzupgo 20 mg/g cream
delgocitinib

2. STATEMENT OF ACTIVE SUBSTANCE(S)

1 g of cream contains 20 mg delgocitinib.

3. LIST OF EXCIPIENTS

Excipients: benzyl alcohol (E 1519), butylhydroxyanisole (E 320), cetostearyl alcohol, citric acid monohydrate (E 330), disodium edetate, hydrochloric acid (E 507), liquid paraffin, macrogol cetostearyl ether, purified water.

4. PHARMACEUTICAL FORM AND CONTENTS

Cream

Multipack: 3 tubes (2 tubes of 15 g and 1 tube of 60 g)

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Cutaneous use

Read the package leaflet before 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

9. SPECIAL STORAGE CONDITIONS

Do not freeze.

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

LEO Pharma A/S
Industriparken 55
DK-2750 Ballerup
Denmark

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/24/1851/003 Multipack containing 3 (2 x 15 g + 1 x 60 g) tubes

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Anzupgo 20 mg/g

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 FOR MULTIPACK (WITHOUT BLUE BOX)

1. NAME OF THE MEDICINAL PRODUCT

Anzupgo 20 mg/g cream
delgocitinib

2. STATEMENT OF ACTIVE SUBSTANCE(S)

1 g of cream contains 20 mg delgocitinib.

3. LIST OF EXCIPIENTS

Excipients: benzyl alcohol (E 1519), butylhydroxyanisole (E 320), cetostearyl alcohol, citric acid monohydrate (E 330), disodium edetate, hydrochloric acid (E 507), liquid paraffin, macrogol cetostearyl ether, purified water.

4. PHARMACEUTICAL FORM AND CONTENTS

Cream

1 tube (15 g)
1 tube (60 g)

Component of a multipack, can't be sold separately.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Cutaneous use

Read the package leaflet before 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

9. SPECIAL STORAGE CONDITIONS

Do not freeze.

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

LEO Pharma A/S
Industriparken 55
DK-2750 Ballerup
Denmark

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/24/1851/003 Multipack containing 3 (2 x 15 g + 1 x 60 g) tubes

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Anzupgo 20 mg/g

17. UNIQUE IDENTIFIER – 2D BARCODE

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGING

TUBE, 60 g

1. NAME OF THE MEDICINAL PRODUCT

Anzupgo 20 mg/g cream
delgocitinib

2. STATEMENT OF ACTIVE SUBSTANCE(S)

1 g of cream contains 20 mg delgocitinib.

3. LIST OF EXCIPIENTS

Excipients: benzyl alcohol (E 1519), butylhydroxyanisole (E 320), cetostearyl alcohol, citric acid monohydrate (E 330), disodium edetate, hydrochloric acid (E 507), liquid paraffin, macrogol cetostearyl ether, purified water.

4. PHARMACEUTICAL FORM AND CONTENTS

Cream

60 g

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Cutaneous use

Read the package leaflet before 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

9. SPECIAL STORAGE CONDITIONS

Do not freeze.

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

LEO Pharma A/S
Industriparken 55
DK-2750 Ballerup
Denmark

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/24/1851/002	60 g
EU/1/24/1851/003	Multipack containing 3 (2 x 15 g + 1 x 60 g) tubes

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

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGING

TUBE, 15 g

1. NAME OF THE MEDICINAL PRODUCT

Anzupgo 20 mg/g cream
delgocitinib

2. STATEMENT OF ACTIVE SUBSTANCE(S)

1 g of cream contains 20 mg delgocitinib.

3. LIST OF EXCIPIENTS

Excipients: benzyl alcohol (E 1519), butylhydroxyanisole (E 320), cetostearyl alcohol, citric acid monohydrate (E 330), disodium edetate, hydrochloric acid (E 507), liquid paraffin, macrogol cetostearyl ether, purified water.

4. PHARMACEUTICAL FORM AND CONTENTS

Cream

15 g

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Cutaneous use

Read the package leaflet before 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

9. SPECIAL STORAGE CONDITIONS

Do not freeze.

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

LEO Pharma A/S (as LEO logo)
Industriparken 55
DK-2750 Ballerup
Denmark

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/24/1851/001	15 g
EU/1/24/1851/003	Multipack containing 3 (2 x 15 g + 1 x 60 g) tubes

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

B. PACKAGE LEAFLET

Package leaflet: Information for the user

Anzupgo 20 mg/g cream
delgocitinib

▼This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

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, pharmacist or nurse.
- 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, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

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

1. What Anzupgo is and what it is used for

Anzupgo contains the active substance delgocitinib. It belongs to a group of medicines called Janus kinase inhibitors.

Anzupgo is used in adults to treat moderate to severe chronic hand eczema. It is used when corticosteroid skin creams do not work well enough or cannot be used.

Anzupgo targets different proteins (enzymes) in the body called Janus kinases. It works by blocking the activity of four specific Janus kinase enzymes, which helps reduce inflammation and immune responses that cause hand eczema. By suppressing these processes, Anzupgo can help to improve the condition of the skin and reduce itching and pain. This, in turn, can increase the ability to perform daily activities and can improve the quality of life.

2. What you need to know before you use Anzupgo

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

Warnings and precautions
Talk to your doctor, pharmacist or nurse before using Anzupgo.

Children and adolescents
Do not use this medicine in children and adolescents below the age of 18 years because it has not been studied in this age group.

Other medicines and Anzupgo
Tell your doctor or pharmacist if you are using, have recently used or might use any other medicines.

Using Anzupgo at the same time as other medicines on the affected skin is not recommended, as it has not been studied.

Pregnancy and breast-feeding
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor for advice before using this medicine.

The effects of this medicine in pregnant women are not known; therefore, it is preferable to avoid the use of Anzupgo if you are pregnant or think you may be pregnant.

It is unknown whether delgocitinib passes into human breast milk, but only very small amounts of this medicine are absorbed into the body. No risk to the baby is therefore anticipated and Anzupgo can be used during breast-feeding.

However, if you are breast-feeding, you should take care that this medicine does not come into contact with your nipple or any other area where your baby may ingest it during feeding.

If you are taking care of a baby, you should also take care to avoid hand contact with the baby's skin immediately after applying Anzupgo. This is a precaution to limit any unnecessary exposure of the baby to this medicine. In the event of accidental transfer of the cream to the baby's skin, the cream can be wiped off.

Driving and using machines
This medicine is not expected to have any effect on your ability to drive or to use machines.

Anzupgo contains benzyl alcohol, butylhydroxyanisole, and cetostearyl alcohol
This medicine contains 10 mg of benzyl alcohol (E 1519) in each gram. Benzyl alcohol may cause allergic reactions or mild local irritation.

Butylhydroxyanisole (E 320) may cause local skin reactions (e.g. contact dermatitis) or irritation to the eyes and mucous membranes.

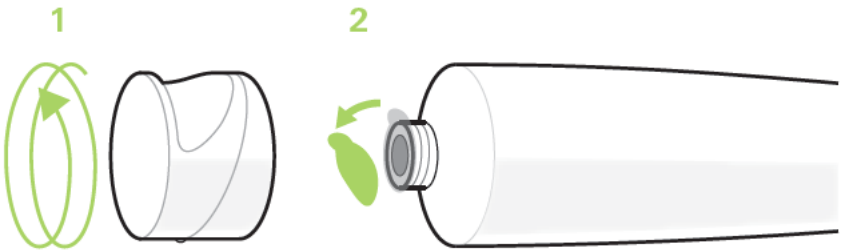
Cetostearyl alcohol may cause local skin reactions (e.g. contact dermatitis).

3. How to use Anzupgo

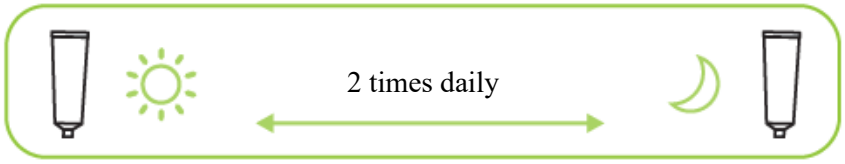
Always use this medicine exactly as your doctor, pharmacist or nurse has told you. Check with your doctor, pharmacist or nurse if you are not sure.

Anzupgo is for use on the skin only. Avoid contact with your eyes, mouth or nose. If the cream gets on any of these areas, thoroughly wipe off and/or rinse off the cream with water.

Before first use
1. Screw off the cap.
2. Peel off the seal at the top end of the tube. Screw the cap back on.



Dose and method of administration
- Avoid applying other products, such as creams or ointments, to the skin immediately before or after application of Anzupgo.
- Apply a thin layer of Anzupgo twice a day to the affected areas of your hands and wrists. Make sure your skin is clean and dry.



If someone else applies this medicine to your skin, they should wash their hands after application.

How long should you use Anzupgo
- You should use Anzupgo until your skin has become clear or almost clear, or as directed by your doctor.
- When instructed by your doctor, you can restart using Anzupgo if signs or symptoms of chronic hand eczema reappear.
- If you do not see any improvement after 12 weeks of treatment with Anzupgo, you should talk to your doctor.

If you use more Anzupgo than you should
If you have applied too much Anzupgo, wipe off the excess.

If you forget to use Anzupgo
If you forget to apply the cream at the scheduled time, do it as soon as you remember and then continue your normal schedule. Do not apply the cream more than twice a day.

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

4. Possible side effects

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

The following side effects have been reported with Anzupgo:

Common (may affect up to 1 in 10 people)
- Application site reactions (i.e., pain, itching, redness, and tingling)

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist or nurse. 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.

5. How to store Anzupgo

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 tube and carton after 'EXP'. The expiry date refers to the last day of that month.

Do not freeze.

The tube should be discarded 1 year after first opening.

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 Anzupgo contains
- The active substance is delgocitinib. Each gram of cream contains 20 mg of delgocitinib.
- The other ingredients are benzyl alcohol (E 1519), butylhydroxyanisole (E 320), cetostearyl alcohol, citric acid monohydrate (E 330), disodium edetate, hydrochloric acid (E 507) (for pH-adjustment), liquid paraffin, macrogol cetostearyl ether, and purified water (see section 2 "Anzupgo contains benzyl alcohol, butylhydroxyanisole, and cetostearyl alcohol").

What Anzupgo looks like and contents of the pack
Anzupgo is a white to slightly brown cream.

Anzupgo is supplied in tubes containing 15 or 60 grams of cream, or in multipacks comprising 3 tubes, 2 tubes containing 15 g each and 1 tube containing 60 g. Not all pack sizes may be marketed.

Marketing Authorisation Holder
LEO Pharma A/S
Industriparken 55
DK-2750 Ballerup
Denmark

Manufacturer
LEO Laboratories Ltd.
285 Cashel Road
Crumlin, Dublin 12
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For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

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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 .