SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Ultracortenol 5 mg/g eye ointment

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

1 g contains: prednisolone pivalate 5 mg.
1 cm string of ointment contains approx. 0.1 mg of prednisolone pivalate.

Excipient(s) with known effect
1 gram of ointment contains 5 mg cetostearyl alcohol and 50 mg wool fat.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Eye ointment

White to slightly yellowish, odourless.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Severe allergic eye inflammation and severe non-infectious inflammatory conditions in the outer parts of the eye and anterior segments.

Ultracortenol 5 mg/g eye ointment is indicated in adults.

4.2 Posology and method of administration

Posology

Adults:

A string of 3-5 mm ointment should be applied 2-4 times daily in the conjunctival sac of the eye.

The maximum daily dose of ointment is a string of 5 mm,4 times daily.

If no improvement is seen within 2 days of initiation of treatment, the indication should be re-evaluated (see Section 4.4). Uncontrolled prolonged use should be avoided. Do not interrupt treatment abruptly but instead reduce the dose gradually over a period of several days or weeks.

The duration of the treatment period should be adjusted individually.

If treatment is longer than 10 days, please see section 4.4 (“Special warnings and precautions for use”).

Treatment with corticosteroids should generally not exceed 4 weeks (see section 4.4). Uncontrolled long-term use must be avoided.

Paediatric population
Safety and efficacy for children have not been established.
The lowest possible dose should be used. Long-term treatment should be avoided in children (see section 4.4).

Method of administration
To be applied in the conjunctival sac of the eye.

Prior to application, contact lenses must be removed and may only be inserted after 15 minutes.

In order to reduce possible systemic absorption, it is recommended that the lacrimal sac at the medial canthus be compressed (punctual occlusion) for 1 minute (see section 4.4). If more than one topical ophthalmic medicinal product is being used, the medicines must be administered at least 5 minutes apart. Eye ointments like Ultracortenol should be administered last.

4.3 Contraindications

- Hypersensitivity to the active substance prednisolone pivalate, other glucocorticoids or to any of the excipients listed in section 6.1
- Acute herpes simplex (dendritic keratitis) and other viral eye infections.
- Acute untreated bacterial or fungal infection of the eye.
- Narrow-angle glaucoma and advanced glaucoma when medicinal products alone do not provide adequate control.

4.4 Special warnings and precautions for use

- After prolonged use, intraocular pressure may rise in predisposed patients (eg. patients with diabetes mellitus). There is a risk that this may develop into glaucoma with damage to the optic nerve leading to visual field defects. Therefore, intraocular pressure should be checked regularly. Especially when using the medicine for 10 days or more, the intraocular pressure and cornea should be checked regularly.
- In case of long-term treatment with topical corticosteroids can cause thinning of the cornea or sclera and risk of perforations.
- Prolonged and intensive treatment can lead to the formation or preheating of subcapsular grey cataracts.
- Acute festering eye infections can be masked when using Ultracortenol or even aggravated by the use of corticosteroids. As Ultracortenol contains no antimicrobial substance, appropriate measures to fight pathogens should be taken if an infection is present.
- The use of corticosteroids can aggravate or cause viral infections of the eye (eg. herpes simplex). Use of ocular ointment containing cortisone in patients who have previously suffered from a herpes simplex infection should be closely monitored. (see also section 4.3).
- Fungal infections of the cornea with the long-term treatment of local corticosteroids occur. Fungal infections can be suspected in all persistent corneal ulcers when a steroid is used or previously used.
- Eye medications containing cortisone can affect wound healing, especially if used for a longer period of time and higher concentration. The use of steroids after a cataract surgery can delay healing and increase the incidence of blister formation.
- After the intensive use of topical steroids, systemic side effects may occur. Punctal occlusion is recommended (see Section 4.2).
- In the case of prolonged high-dose of topical steroids, the risk of adrenal suppression must be taken into account, especially in children. Visual disturbance can be reported with systemic and topical use of corticosteroids. Consider referring a patient with symptoms such as blurred vision or other visual disturbances, to an ophthalmologist for investigation of possible causes. These may include cataracts or rare diseases such as central serous chorioretinopathy (CSCR), which have been reported following use of systemic and topical corticosteroids.
- Cetostearyl alcohol and wool fat can cause local skin irritation (e.g. contact dermatitis).

- Contact lenses should be removed before application and not re-inserted until after at least 15 minutes after application.
- To prevent contamination of the drug and injury, make sure that the dosing tip does not touch the eye, the eyelid or the area around the eye or any other objects.

4.5 Interactions with other medicinal products and other forms of interaction

No formal interaction studies have been conducted.

A further increase in intraocular pressure cannot be excluded if eye drops containing corticosteroid are administered simultaneously with substances such as atropine or other anticholinergic agents that may also increase intraocular pressure in predisposed patients.

In the case of simultaneous treatment with CYP3A inhibitors including products containing cobicistat, an increased risk of systemic side effects is possible. Any combination should be avoided, unless the use outweighs the risk of systemic side effects caused by corticosteroids. In this case, patients should be monitored with regard to systemic corticosteroid-induced side effects.

The concurrent use of topical corticosteroids and NSAIDs has been identified as a risk factor for the development of corneal erosion and potential perforation.

4.6 Fertility, Pregnancy and lactation

Pregnancy

There are no or limited amount of data from topical use of eye cream with prednisolone in pregnant women. After systemic use of corticosteroids, effects on unborn / newborn (intrauterine growth retardation, adrenal cortex suppression) have been reported. Studies in animals have shown reproductive toxicity following systemic administration of corticosteroids (see section 5.3). The relevance in human is unknown. Therefore, this medicine should be used with caution during pregnancy and only if the possible benefit to the mother outweighs the potential risk to the fetus.

Breast-feeding

Prednisolone is excreted in human milk, but at therapeutic doses it seems unlikely that there will be any effects on the child. Ultracortenol can be used during breastfeeding.

Fertility

Animal studies have shown that high systemic exposure to corticosteroids impair fertility (see section 5.3)

4.7 Effects on ability to drive and use machines

After administration, the patient may experience temporary blurred vision which may affect the ability to drive or use machines. Patients who are affected should not drive or use machines until vision is clear.

4.8 Undesirable effects

The short-term treatment of the eye with locally applied prednisolone is safe and well tolerated.

The risk of adverse reactions is low. Furthermore, relevant systemic side effects are not expected after appropriate use of Ultracortenol.

The results from the clinical assessment support that the use of Ultracortenol is efficacious and safe.

The medicinal products Ultracortenol produce substantial therapeutic benefit while maintaining a highly favorable safety profile.

The following side effects have been observed and reported during treatment with prednisolone at the following frequencies:

Common: (≥1/100 to <1/10);
Uncommon: (≥1/1.000 to <1/100);
Rare: (≥1/10.000 to <1/1000);
Not known (cannot be estimated from available data)

Side effects				
System Organ Class	Common	Uncommon	Rare	Not known
Central and peripheral nervous system				Headache
Immune system				Hypersensitivity, urticaria
Eye	Increased intra-ocular pressure in case of long-term treatment, burning sensation, stinging, eye irritation, and feeling of having something in the eye.	Blurred vision	Penetrating eye injury (scleral or corneal perforation), cataract (also sub-capsular), allergic reactions.	Eye infection (including bacterial, fungal and viral infection), mydriasis.
Gastro-intestinal tract				Dysgeusia
skin and skin cellular tissue				Pruritus, exanthema

The following side effects have been reported for drugs in the same group (corticosteroids) when used for the treatment of eye diseases

Rare (see also section 4.4): Acute external uveitis (iritis), keratitis, conjunctivitis, difficulty in accommodation, ptosis

Increased intraocular pressure occurs in some people, mainly during prolonged treatment. Corneal perforation occurs mainly in the long-term treatment of diseases that cause thinning of the cornea (see also section 4.4).
In case of prolonged topical application of corticosteroids (especially in children), undesirable effects may occur.

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

Symptoms
In general, acute toxicity does not present any clinical problems, even in case of massive doses. There is a possibility that acute overdosing may occur without aggravating pre-existing conditions such as ulcers, electrolytic disorders, infections, edema. Repeated high doses of methyl-prednisolone have caused liver necrosis and increased amylase levels. Brady arrhythmia, ventricular arrhythmia and cardiac arrest were observed on administration of high doses of methyl-prednisolone and dexamethasone.

Management
Usually, not required. See Symptomatic treatment for approved gastric lavage.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Ophthalmologicals, Corticosteroids, Plain. ATC-code: S01BA04.

Prednisolone acetate is a synthetic gluco-corticoid with anti-inflammatory effect about 4 times stronger than hydrocortisone. It prevents the release of prostaglandins and leukotrienes, which are inflammatory mediators, by inhibiting arachidonic acid synthesis. Therefore, the medicine counteracts acute inflammatory manifestations such as edema, fibrin accumulation, vasodilation, phagocytic migration, collagen accumulation and scarring.

5.2 Pharmacokinetic properties

Absorption:

Locally administered ocular prednisolone is absorbed into the aqueous humour. Maximum aqueous concentrations are reached within 2 and 4 hours after application of prednisolone acetate and prednisolone sodium phosphate drops.

Negligible systemic exposure is expected after topical application using eye ointment.

Elimination:

Prednisolone is metabolized, which is known to occur not only in the liver but also local peripheral tissues. The haslf-life in the aqueous humourist estimated to be about 30 minutes.

Interactions

Systemic exposure of prednisolone following local application in the eye is expected to be negligible.

5.3 Pre-clinical safety data

In animal studies, methods of administration that have resulted in a high systemic exposure of corticosteroids have been shown to give rise to malformations of various kinds (cleft palate, skeletal malformations). After long-term treatment, reduced placental and birth weight have been observed in animals.
Corticosteroids have been shown to reduce fertility following high systemic exposure in rats.

Topical administration of prednisolone for 6 months in rabbits resulted in reduced body weight gain and reduced size of liver, adrenals and thyroid, however the kidney and spleen size increased. Chronic pyelonephritis and increased IOP were also reported which were normalised after 4 weeks of treatment with prednisolone.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

cetostearyl alcohol;
wool fat;
paraffin, white soft;
paraffin, liquid;
water, purified.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

4 years

Opened package: Use within 4 weeks after first opening.

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

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

6.5 Nature and contents of container

5 g white to slightly yellowish odourless ointment in an epoxy-phenol coated aluminium tube with white HDPE canula tip and white HDPE screw cap.

6.6 Special precautions for disposal

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

7 MARKETING AUTHORIZATION HOLDER

<To be completed nationally>

8 MARKETING AUTHORIZATION NUMBER(S)

<To be completed nationally>

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

<To be completed nationally>

10 DATE OF REVISION OF THE TEXT

17 June 2022