SUMMARY OF PRODUCT CHARACTERISTICS

1. Name of the Medicinal Product

Neopred Ophthalmic Emulsion

Difluprednate Ophthalmic Emulsion, 0.05% w/v

2. Qualitative and Quantitative Composition

Each ml contains Difluprednate INN 0.5 mg

3. Pharmaceutical Form

Ophthalmic Suspension

4. Clinical Particulars

4.1 Therapeutic indications

Neopred Ophthalmic Emulsion is a topical corticosteroid that is indicated for:

- The treatment of inflammation and pain associated with ocular surgery.
- The treatment of endogenous anterior uveitis.

4.2 Posology and method of administration

Posology

For the treatment of inflammation and pain associated with ocular surgery: instill 1 drop into the conjunctival sac of the affected eye 4 times daily beginning 24 hours after surgery and continuing throughout the first 2 weeks of the postoperative period, followed by 2 times daily for a week and then a taper based on the response.

For the treatment of endogenous anterior uveitis: instill 1 drop into the conjunctival sac of the affected eye 4 times daily for 14 days followed by tapering as clinically indicated.

Geriatric Use

No overall differences in safety or effectiveness have been observed between elderly and younger patients.

Pediatrics Use

The safety and efficacy of Difluprednate Ophthalmic Emulsion have not been studied in children (0-3 years of age).

Renal Insufficiency & Hepatic Insufficiency

There were no specific studies in patients with renal insufficiency or with hepatic insufficiency.

Method of administration

For ocular use only.

After the bottle cap is removed, if the tamper evident snap collar is loose, remove before using the product. To prevent contamination of the dropper tip and emulsion, care must be taken not to touch the eyelids, surrounding areas, or other surfaces with the dropper tip of the bottle. Keep the bottle tightly closed when not in use.

In case of concomitant therapy with other topical ocular medicines, an interval of five minutes should be allowed between successive applications. Eye ointments should be administered

4.3 Contraindications

Difluprednate ophthalmic emulsion is contraindicated in most active viral diseases of the cornea and conjunctiva, including epithelial herpes simplex keratitis (dendritic keratitis), vaccinia, and varicella, and also in mycobacterial infection of the eye and fungal disease of ocular structures.

4.4 Special Warnings and Precautions for Use

- For ophthalmic use only.
- If this product is used for 10 days or longer, intraocular pressure should be monitored.
- Fungal infections of the cornea are particularly prone to develop coincidentally with long-term use of steroid topically.
- Prolonged use of corticosteroids may result in glaucoma with damage to the optic nerve, defects in visual acuity & visual field, and in posterior subcapsular cataract formation.
- Use of a corticosteroid medication in the treatment of patients with a history of herpes simplex requires great caution.

4.5 Interaction With Other Medicinal Products

Specific interaction studies have not been conducted with Difluprednate ophthalmic emulsion.

Topical ophthalmic corticosteroids and nonsteroidal anti-inflammatory drugs (NSAIDs) are known to slow or delay healing. Concomitant use of topical steroids and topical NSAIDs may increase the potential for healing problems.

The preservative in Difluprednate ophthalmic emulsion, sorbic acid, can interact with soft contact lenses. Difluprednate ophthalmic emulsion should not be instilled while wearing contact lenses.
Drug-drug, Drug-Food, Drug-Herb, Drug-Laboratory, Drug-Lifestyle interactions were not studied

4.6 Fertility, Pregnancy and Lactation

Effects on Fertility

Difluprednate was embryotoxic, and teratogenic in animals. The effect of subcutaneous administration of difluprednate during the reproductive and early embryonic development period in rats was examined (Fertility and Early Embryonic Development). No effects on the reproductive potential and embryonic development were noted in the rats at 0.1 μg/kg, but at 10.0 μg/kg suppression of body weight gain, a decrease in food intake, and a decrease in thymus weight were noted in both male and female rats before mating; these changes were accompanied by a decrease in embryonic body weights and a delay in embryonic ossification. There were no observed abnormalities in the estrous cycle or copulation and fertility rates, and there were no differences in the number of corpora lutea, weight of the placenta, number of implantations, and number of dead embryos (zero in all groups) between the 3 treatment groups and the control group. Also, no embryonic abnormalities in the viscera, bones, or general appearance occurred as a result of difluprednate exposure

4.7 Effects on ability to drive and use machines

Difluprednate ophthalmic emulsion may cause temporary blurred vision or other visual disturbances, which may affect the ability to drive or use machines. If blurred vision occurs after instillation, the patient should be advised to wait until vision clears before driving or using machinery.

4.8 Undesirable effects

Ocular adverse events generally associated with ophthalmic steroids may include elevated intraocular pressure (IOP) which can be associated with optic nerve damage, punctate keratitis, visual acuity and field defects, posterior subcapsular cataract formation, secondary or reactivation of ocular infection from pathogens including herpes simplex, delayed wound healing, corneal effects, and perforation of the globe where there is thinning of the cornea or sclera.

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 requested to report any suspected adverse reactions to the national Regulatory Authorities

4.9 Overdose

There were no cases of overdose reported. There is no specific antidote for Difluprednate ophthalmic emulsion overdose. A topical overdose is not likely to be associated with toxicity.

5.0 Pharmacological Properties

5.1 Pharmacodynamic Properties ATC

Code: S01BA16

Mechanism of action

Corticosteroids inhibit the inflammatory response to a variety of inciting agents and may delay or slow healing. They inhibit edema, fibrin deposition, capillary dilation, leukocyte migration, capillary proliferation, fibroblast proliferation, deposition of collagen, and scar formation associated with inflammation. There is no generally accepted explanation for the mechanism of action of ocular corticosteroids. However, corticosteroids are thought to act by the induction of phospholipase A2 inhibitory proteins, collectively called lipocortins. It is postulated that these proteins control the biosynthesis of potent mediators of inflammation such as prostaglandins and leukotrienes by inhibiting the release of their common precursor arachidonic acid. Arachidonic acid is released from membrane phospholipids by phospholipase A2.

5.2 Pharmacokinetic Properties

Difluprednate (DFBA, 6α,9-difluoro-11β,17,21,-trihydroxypregna-1,4-diene-3,20-dione 21-acetate 17-butyrate) undergoes deacetylation *in vivo* to 6α,9-difluoroprednisolone 17-butyrate (DFB), an active metabolite of difluprednate.

Clinical pharmacokinetic studies of difluprednate after repeat ocular instillation of 2 drops of difluprednate (0.01% or 0.05%) four times per day for 7 days showed that DFB levels in blood were

below the quantification limit (50 ng/mL) at all-time points for all subjects, indicating the systemic absorption of difluprednate after ocular instillation of Difluprednate ophthalmic emulsion is limited.

The binding of radiolabeled difluprednate to human serum protein has been determined to be 73% in vitro.

3 Preclinical safety data

Carcinogenesis, Mutagenesis, Impairment of Fertility

Difluprednate was not genotoxic in vitro in the Ames test, and in cultured mammalian cells CHL/IU (a fibroblastic cell line derived from the lungs of newborn female Chinese hamsters). An in vivo micronucleus test of difluprednate in mice was also negative. Treatment of male and female rats with subcutaneous difluprednate up to 10 mcg/kg/day prior to and during mating did not impair fertility in either gender. Long-term studies have not been conducted to evaluate the carcinogenic potential of difluprednate.

Animal Toxicology and/or Pharmacology

In multiple studies performed in rodents and nonrodents, subchronic and chronic toxicity tests of difluprednate showed systemic effects, such as suppression of body weight gain; a decrease in lymphocyte count; atrophy of the lymphatic glands and adrenal gland; and for local effects, thinning of the skin; all of which were due to the pharmacologic action of the molecule and are well known glucocorticosteroid effects. Most, if not all of these effects were reversible after drug withdrawal. The NOEL for the subchronic and chronic toxicity tests were consistent between species and ranged from 1-1.25 mcg/kg/day.

6. Pharmaceutical Particulars

6.1 List of excipients

- Glycerin
- Polyoxyl 35 Castor Oil
- Polysorbate 80 (Tween 80)
- Povidone (K-17)
- Sorbic Acid
- Aminocaproic Acid
- Mannitol
- Disodium Hydrogen Phosphate Dihydrate
- Sodium Hydroxide or Hydrochloric Acid for pH adjustment
- Water for Injections

6.2 Incompatibilities

Not applicable

6.3 Shelf life

2 years

6.4 Special precautions for storage

- Store below 25ºC
- Protect from light.
- Discard 30 days after opening.
- Keep out of the reach of children.

6.5 Nature and contents of container

Low Density Polyethylene (LDPE) white opaque dropper bottle with a LDPE white opaque dropper tip and High Density Polyethylene (HDPE) white opaque screw cap.
Pack size: 5 ml

6.6 Special precautions for disposal and other handling

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

7. Marketing Authorization Holder

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8. Marketing Authorization Numbers

CTD13417

9. Date of first Authorization/renewal of Authorization

10/06/2026

10. Date of revision of the text

10/06/2026