SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

DIFENASOL 0.1 % eye drops, solution

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active ingredient: 0.1% w/v sodium diclofenac.
For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Eye drops solution.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

- Inhibition of perioperative miosis during cataract surgery
- Prevention of post-operative inflammation in cataract and eye anterior segment surgery
- Ocular pain treatment during the 24 hours following photorefractive keratectomy surgery

4.2 Posology and method of administration

Posology
Adults
- Inhibition of preoperative miosis during cataract surgery: 1 drop up to 5 times during the 3 hours before surgery.
- Prevention of post-operative inflammation in cataract and eye anterior segment surgery:
    - Pre-operatively: 1drop up to 5 times during the 3 hours before surgery
    - Post-operatively: 1 drop 3 times immediately after surgical intervention, then one drop 3 to 5 times daily. Treatment duration should not exceed 4 weeks.
- Control of post-photorefractive keratectomy pain and discomfort:
    - Pre-operatively: 2 drops in the hour prior to surgery
    - Post-operatively: 2 drops immediately after surgery and then 4 drops during the 24 post-operative hours.

1. With the spike: tighten the cap on the nozzle.
2. The spike in the cap will pierce the tip of the bottle.
3. Dispense drops with gentle pressure. Replace the cap after every use.

Paediatric use
No specific studies for use in children are available;

Elderly patients
In these patients no dose adjustment is required

Method of administration

Ocular use. To be applied locally in the eye in the inferior conjunctival fornix.

Patients should be advised to:

- Carefully wash hands before using the drops.
- Avoid any contact between the nozzle and the eye or eyelid.
- Recap the bottle after use.

In case of concomitant use with other eye drops, an interval of 15 minutes between each application should be maintained to prevent the dilution of active substances.

4.3 Contra-indications

This medicine is contra-indicated in case of hypersensitivity to diclofenac sodium or to any of the excipients, in case of history of allergy, urticaria, acute rhinitis or asthma triggered by diclofenac sodium intake or by other drugs with a similar activity, such as aspirin and the other non steroidal anti-inflammatory drugs (NSAIDs) (see section 4.4).

4.4 Special warnings and precautions for use

Do not inject, do not swallow.
This eye drops solution is not intended for peri ocular or intra ocular injection.
Difenasol, as others NSAIDs, may induce in rare cases allergic reactions including anaphylactic reactions, even without prior exposure to the drug. Cross hypersensitivity reactions with acetylsalicylic acid and the others NSAIDs are possible (see section 4.3).
In case of hypersensitivity reactions such as itching, redness or signs suggesting allergy including asthma attack or sudden swelling of the face and the neck, the treatment should be discontinued.
Patients with asthma associated with chronic rhinitis, chronic sinusitis and /or nasal polyps have a higher risk to have allergic reactions during administration of acetylsalicylic acid and/or others NSAIDS.
The anti-inflammatory activity of ophthalmic NSAIDs may mask the onset and/or progression of ocular infections. NSAID has no antimicrobial properties. In case of ocular infection, caution should be exercised when topical NSAIDs are used concomitantly with antibiotics.
Topical NSAIDs, such as diclofenac, may delay corneal epithelium healing even when there are used during a short time period. The consequences of delayed corneal healing on the cornea quality and on the risk of infection are not clear. Topical steroids are also known to slow down and delay healing. The concomitant use of topical steroids with topical NSAIDs may increase the risk of problems during healing.
As NSAIDs may increase the risk of bleeding during eye surgery, it is recommended to use this medicine with care in patients with history of bleeding or in patients receiving other medications which may prolong bleeding time.
When patients are treated with high doses for a prolonged period of time, topical NSAIDs may induce keratitis. In some sensitive patients, the continuous use of topical NSAIDs may lead to corneal thinning, corneal epithelium defect, and ulcerative keratitis which might become sight-threatening.
As this medicine contains benzalkonium, it may cause eyes irritation. Avoid contact with soft contact lenses, remove contact lenses prior to application and wait at least 15 minutes before reinsertion. Benzalkonium chloride is known to discolour soft contact lenses.

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies are available.

4.6 Pregnancy and lactation

Pregnancy
There are no data on the use of diclofenac eye drops solution in pregnancy. Studies in animals with diclofenac have shown reproduction toxicity at maternally toxic dose (see section 5.3).
The effects of diclofenac on fertility, foetal development and delivery as well as postnatal development are pharmacological consequences of prostaglandin synthesis inhibition.
Although very low systemic exposure is expected after administration of diclofenac eye drops during pregnancy, Difenasol should only be used when clearly necessary and only at the lowest effective doses for the shortest duration.

First trimester, it is preferable not to use this medicine during the first 12 weeks of absence of menstruation.
From 2.5 to 5 complete months (between 12 and 24 weeks of absence of menstruation), this medicine is partially contra-indicated, it is to be used for a limited period.
After 5 complete months (24 weeks of absence of menstruation), do not use this medicine, because it can have serious consequences on the child, especially cardio-pulmonary and renal, even after one application.

Lactation
As diclofenac is excreted in mother's milk (breast milk) at very low level, no effects on the sucking child are anticipated. Difenasol can be used during breastfeeding.

4.7 Effects on ability to drive and use machines

A transient blurred vision may occur immediately after instillation of Difenasol eye drops. Patients with blurred vision should refrain from driving a vehicle or operating machines.

4.8 Undesirable effects

Infections and infestations
Not known frequency: rhinitis

Immune system disorders
Rare (≥1/10,000, <1/1000): hypersensitivity

Eye disorders:

Uncommon (≥1/1000, <1/100): a slight transient burning sensation and blurred vision immediately after instillation of eye drops

Rare (≥1/10,000, <1/1000): punctuate keratitis, corneal thinning, and ulcerative keratitis
Not known frequency: conjunctival hyperaemia, allergic conjunctivitis, eyelid oedema

Respiratory, thoracic and mediastinal disorders
Rare (≥1/10,000, <1/1000): dyspnoea and exacerbation of asthma

Not known frequency: cough

Skin and subcutaneous tissue disorders
Rare (≥1/10,000, <1/1000):pruritis, erythema, hypersensitivity reactions
Not known frequency: urticaria, rash, eczema.

In patients with risk factors of corneal disorders such as during the use of corticosteroids or with concomitant diseases such as infections or rheumatoid arthritis, diclofenac has been associated, in rare cases, with ulcerative keratitis, corneal thinning. Most patients were treated for a prolonged period of time.
Post marketing data suggest that patients with surgical ophthalmic complications, corneal epithelium defects, diabetes, disease of the eye surface (dry eye syndrome), rheumatoid arthritis, repeated eye surgeries during a short period of time, may have a higher risk in corneal adverse reactions.
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.

4.9 Overdose

Not applicable.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: antiinflammatory agents, non steroid , ATC code: S01BC03
Diclofenac sodium is a non steroidal anti-inflammatory drug (NSAID) with analgesic properties. Diclofenac sodium inhibits cyclooxygenase (COX) involved in the prostaglandin synthesis. Diclofenac is also an antipyretic, an anti aggregating agent and a cytochrome 450 CYP 2C9 substrate. Diclofenac sodium has been shown to inhibit miosis during cataract surgery, to reduce inflammation following surgical interventions, trauma and other inflammatory affections.

5.2 Pharmacokinetic properties

In rabbits, peak concentrations of 14C-labelled diclofenac are achieved in the cornea and conjunctiva 30 minutes after application. Elimination was fast and almost complete after 6 hours. Penetration of diclofenac into the anterior chamber has been confirmed in humans. No measurable levels of diclofenac could be found in humans after ocular application of diclofenac sodium eye drops.

5.3 Preclinical safety data

During repeated dose toxicity studies, the most frequently observed adverse effects were gastrointestinal disorders, such as ulcerations, at oral dosage of 0.5 to 2.0 mg/kg according to species (namely 300 to 1200 times the ocular daily dose in humans).
In reproductive toxicity studies in animals, embryo-foetotoxicity, prolonged gestationand dystocia have been observed.

Whilst no teratogenic effects have been demonstrated, maternally toxic dose were associated with decreased foetal survival, and intrauterine growth retardation.
After up to 3 months of repeated instillations of diclofenac 1mg/ml in rabbits eyes, no adverse effect has been observed.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Boric acid; disodium edetate; benzalkonium chloride; polyoxyl 35 castor oil; tromethamine; water for injections.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Store at room temperature (below 30°C). Protect from light.
Do not use after one month after the bottle opening.
Keep out of the reach and sight of children.

6.5 Nature and contents of container and special equipment for use, administration or implantation

Bottle of 5 ml made of LDPE 5 low density polyethylene)

6.6 Special precautions for disposal and handling

Not applicable

7. CATEGORY OF DISTRIBUTION:

☐ Over-the counter medicine ☒ Prescription only medicine

List II

8. MARKETING AUTHORISATION HOLDER

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9. MANUFACTURER

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10. DATE OF REVISION OF THE TEXT

January 2019