SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Dicloftil 0.1% eye drops, solution – 30 single-dose containers 0.5 ml

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

100 ml contain
100 mg of diclofenac sodium (equal to 93.084 mg of diclofenac).
One ml of Dicloftil 0.1% eye drops contains 1 mg of diclofenac sodium.

Excipient(s) with known effect(s): boric acid.

For a complete list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Eye drops, solution in single-dose containers.

4. CLINICAL INFORMATION

4.1 Therapeutic indications

• Post-operative inflammation following cataract extraction.
• Control of ocular pain and discomfort associated with corneal epithelial defects after laser excimer PRK surgery or accidental trauma.

4.2 Posology, dosage and method of administration

Adults

a) Ocular surgery and its complications

Preoperatively, up to 1 drop 5 times during the 3 hours before surgery.
Postoperatively, 1 drop 3 times on the day of surgery, followed by 1 drop 3 to 5 times daily for as long as required.

b) Treatment of pain and discomfort

One drop 4 to 6 hourly.
When pain is due to a surgical procedure (e.g. refractive surgery(. Instill 1 drop, 30-60 minutes prior to surgery, into the eye to be operated on. During the first 10 minutes following surgery, instill 1-2 doses of 1 drop each, followed by 1 drop 4 times daily for 2 days.

Elderly: There is no indication that dosage needs to be modified for the elderly.

Paediatric use:
Dicloftil 0.1% eye drops is not indicated for use in children. Paediatric experience is limited to a few published clinical studies in strabismus surgery.
The dispenser remains sterile until the original closure is broken. Patients must be instructed to avoid allowing the tip of the dispensing container to to contact the eye or surrounding structures as this may contaminate the solution.
If more than one medication needs to be instilled in the eye, an interval of at least 5 minutes between application of the different medicinal products must be allowed.
Following instillation of the eye drops, nasolacrimal occlusion or closing the eyes for
3 minutes may reduce systemic absorption. This may result in a decrease in systemic side effects and an increase in local activity.

4.3 Contraindications
- Hypersensitivity to the active ingredient or to any of the excipients listed in section 6.1;
- hypersensitivity to other non-steroidal anti-inflammatory drugs (NSAIDs) (such as acetylsalicylic acid, indomethacin, etc.);
- children and adolescents under 14 years of age;
- patients in whom asthmatic attacks, urticaria or acute rhinitis have occurred after taking acetylsalicylic acid or other prostaglandin-synthetase inhibitor drugs.

4.4 Special warnings and precautions for use
For better absorption of the product, an interval of at least 5 minutes should be allowed between the application of Dicloftil and that of another medicinal product.
If infection is present, or if there is a risk of infection, appropriate therapy (e.g., antibiotics) should be administered concurrently with Dicloftil.
In patients who have an increased risk of corneal disease, for example during steroid use, and in patients with concomitant diseases such as rheumatoid arthritis, diclofenac use has been associated in rare cases with the occurrence of ulcerative keratitis or corneal thinning, punctate keratitis, corneal epithelial defects, and corneal edema. Most patients who presented with these complications were treated for a very long period of time.
Topical nonsteroidal anti-inflammatory drugs (NSAIDs) such as diclofenac should be administered with caution in conjunction with topical steroids (see section 4.5).

This medication contains boron and may impair fertility in the future.

4.5 Interactions with other medicinal products and other forms of interaction
Concomitant use of topical nonsteroidal anti-inflammatory drugs such as diclofenac and topical steroids in patients with significant pre-existing corneal inflammation may increase the risk of developing corneal complications, so such use should be done with caution.

4.6 Pregnancy, Lactation and Fertility

Pregnancy
There are no data on the use of diclofenac eye drops in pregnant women. No reproductive toxicity studies have been conducted with diclofenac-based eye drops. However, in animals, systemically administered diclofenac crossed the placental barrier, leading to prolonged gestation and producing embryotoxicity, but showed no teratogenic potential (see section 5.3). Dicloftil eye drops should be applied only in the first and second trimesters of pregnancy and if strictly necessary.
In the third trimester, Dicloftil should not be used because of the risk of premature closure of the ductus arteriosus, pulmonary hypertension and/or renal dysfunction in the fetus, as well as possible prolongation of bleeding time in mother and child and inhibition of uterine contractions in the mother.

Breastfeeding
After oral administration of 50 mg coated tablets, traces of the active ingredient were found only in breast milk and in such low amounts that no adverse reactions occurred in the infant. Ocular use of diclofenac is not recommended during lactation unless the expected benefits outweigh the potential risks.

Fertility
This medication contains boron and may impair fertility in the future.

4.7 Effects on ability to drive vehicles and operate machinery.

Dicloftil 0.1% eye drops, solution impairs the ability to drive vehicles or operate machinery in patients with scotomas.

4.8 Undesirable Effects

The following side effects associated with the use of diclofenac-containing eye drops have been reported:

Occasionally
- Mild to moderate transient burning sensation and/or scotomas immediately after instillation of eye drops.

Other effects observed less frequently
- Ocular pain and blurred vision immediately after instillation of eye drops.

Rarely
- Hypersensitivity reactions with itching and redness, photosensitivity,
- dyspnea and exacerbation of asthma,
- corneal thinning and ulcers (see section 4.4).

Side effects with unknown frequency
- urticaria,
- rash,
- eczema,
- erythema,
- itching,
- hypersensitivity,
- cough,
- rhinitis.

Eye Pathologies
- ulcerative keratitis, punctate keratitis and corneal disorders (corneal thinning, epithelial defects, corneal edema) normally after frequent instillations
- conjunctival hyperemia,
- allergic conjunctivitis,
- eyelid erythema,
- ocular allergy,
- eyelid edema,
- itching of the eyelids,
- burning sensation in the eye.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product.
Any suspected adverse event should be reported to the Ministry of Health according to the National Regulation by using an online form https://sideeffects.health.gov.il/

4.9 Overdose
There are no known overdose events.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic Properties

Pharmacotherapeutic group: ophthalmologic, anti-inflammatory ATC Code: S01BC03
The active ingredient of Dicloftil is diclofenac sodium, a non-steroidal anti-inflammatory drug characterized by an intense antiphlogistic and analgesic activity.
In clinical studies, Dicloftil has been shown to inhibit miosis during cataract surgery, reduce inflammation following surgery and trauma or that present in other non-septic inflammatory states. In addition, a clinical trial demonstrated that Dicloftil administered prophylactically to patients who had undergone cataract lens

extraction and intraocular lens implantation reduced the frequency of occurrence and intensity of cystoid macular edema.
Daily doses of Dicloftil that are effective by conjunctival instillation (approximately 0.25-0.5 mg diclofenac sodium) correspond to less than 1% of the recommended systemic daily dose recommended for rheumatic indications.

5.2 Pharmacokinetic Properties
Peak concentrations in the cornea and conjunctiva were evident 30 minutes after instillation of 14C-labeled diclofenac in the rabbit; elimination was rapid and virtually complete after 6 hours. Penetration of diclofenac into the anterior chamber was also confirmed in humans.
No measurable plasma levels of diclofenac sodium were detected after ocular instillation of Dicloftil in humans.

5.3 Preclinical Safety Data
Preclinical data reveal no special risk to humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential, and reproductive and developmental toxicity.
The LD50 of diclofenac, administered intravenously, in mouse, rat and rabbit is greater than 100 mg/Kg and therefore the acute toxicity is very low. Even orally and for repeated doses up to 4 mg/Kg/day no toxic phenomena were observed.
The local tolerability in the rabbit eye, for single and repeated doses, proved to be good even for concentrations of 0.5% of diclofenac sodium and for long periods of administration, up to 90 consecutive days (4 doses/day).

6. PHARMACEUTICAL INFORMATION

6.1 List of Excipients
Arginine, boric acid, borax, povidone, macrogolglycerol ricinoleate, disodium edetate, and water for injections.

6.2 Incompatibility
In the absence of compatibility studies, this medication should not be mixed with other medications.

6.3 Special precautions for storage
The expiry date of the product is indicated on the packaging materials
Do not store above 25°C.
Do not use the product beyond the expiration date stated on the package.
After opening the box, open the pouch containing 5 single-dose containers, the product should not be used beyond 28 days after opening the pouch (when the single dose container is close).
Dicloftil single-dose should be used immediately after opening the single-dose container.
Discard the single-dose container and any remaining amount of product immediately after use.

6.4 Nature and content of container
Eye drops, solution. 30 single-dose polyethylene containers, 0.5 ml.

6.5 Instructions for use and handling, and disposal
No special instructions.
Unused medicinal product and waste derived from it should be disposed of in accordance with applicable local regulations.

7. Manufacturer
Farmigea S.p.A. Pisa, Italy

8. Registration holder
Bio-Avenir Ltd.
1 David Hamelech ST., Herzelia Pituach 4666101, Israel

9. Registration number of the medicine in the Ministry of Health's National Drug Registry:
138 87 31465 00

Revised in April 2022 according to MOH guidelines.

Diclo -SPC- 0422-01