SUMMARY OF PRODUCT CHARACTERISTICS

1. NAAM VAN HET GENEESMIDDEL

Diclofenac Devatis 1 mg/ml, oogdruppels, oplossing, verpakking voor éénmalig gebruik

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains 1 mg diclofenac sodium

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FROM

Eye drop, solution.
Clear and colourless solution. Free of particles.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

- Prevention of postoperative inflammation in cataract surgery.
- Maintenance of mydriasis during cataract surgery.
- Treatment of ocular pain in photorefractive surgery for up to the 24 first post-operative hours.

4.2 Posology and method of administration

Ocular use

Posology

Adults

Inhibition of miosis during cataract surgery
- Pre-operatively: one drop in the affected eye 3 to 5 times during the 1-2 hours before surgery.

Prevention of inflammation in cataract and anterior eye segment surgeries:
- Pre-operatively: one drop in the affected eye 3 to 5 times during the 1-2 hours before surgery;
- Post-operatively: one drop in the affected eye three to five times daily. A treatment duration exceeding 4 weeks is not recommended.

Treatment of ocular pain in photorefractive surgery for up to the 24 first postoperative hours:
- Pre-operatively: one drop two times in the affected eye within the hour prior to surgery;
- Post-operatively: one drop two times within the hour following surgery and then one drop four times within the 24 post-operative hours.

Paediatric population

Diclofenac Devatis is not indicated for the use in children. There is only limited experience in children aged 2 years and older from clinical studies on strabismus surgery.

Method of administration

Patients should be instructed to avoid contact between the tip of the single-dose container and the eyes or areas around the eyes.

The solution from one individual single dose container of Diclofenac Devatis is to be used immediately after opening since sterility cannot be maintained after the individual single dose container is opened.

When using nasolacrimal occlusion for 1 minute, the systemic absorption is reduced. This may result in a decrease in systemic side effects and an increase in local activity.
If other eye drops are co-administered, wait for about 5 minutes between the instillations (see section 4.5).

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
- History of allergy, attacks of asthma, urticaria or acute rhinitis precipitated by acetylsalicylic acid or by other non-steroidal anti-inflammatory agents (NSAIDs) (see section 4.4).

4.4 Special warnings and precautions for use

Like other NSAIDs, diclofenac may in rare cases induce allergic reactions including anaphylactic reactions, even without prior exposure of the drug. There is a potential for cross-sensitivity with acetylsalicylic acid, phenylacetic acid derivatives and other non-steroidal anti-inflammatory drugs.

Use of topical NSAIDs may result in keratitis. In some susceptible patients, the use of topical NSAIDs may result in epithelial breakdown, corneal thinning, corneal erosion, corneal ulceration or corneal perforation. Post-marketing experience with topical NSAIDs suggests that patients with complicated ocular surgeries, corneal denervation, corneal epithelial defects, diabetes mellitus, ocular surface diseases (e.g., dry eye syndrome), rheumatoid arthritis or repeat ocular surgeries may be at increased risk for corneal adverse reactions within a short period of time. These events may be sight threatening. Prolonged use of topical NSAIDs may increase patient risk for occurrence and severity of corneal adverse reactions. Patients with evidence of corneal epithelial breakdown should immediately discontinue use of Diclofenac Devatis and should be monitored closely for corneal health.

NSAIDs, including diclofenac for topical use, delay the corneal reepithelialization, even with short-term use. The consequences of this for the quality of the cornea and the risk of infection due to the delayed wound healing of the cornea are unclear.

Caution should be exercised when topical NSAIDs such as diclofenac are used concomitantly with topical steroids (see section 4.5).

The anti-inflammatory activity of ophthalmic non-steroidal anti-inflammatory agents (NSAIDs) may mask the onset and/or progression of ocular infections. In the presence of infection, or if there is a risk of infection, appropriate therapy (e.g. antibiotics) should be given concurrently with Diclofenac Devatis.

There have been reports that ophthalmic NSAIDs may cause increased bleeding of ocular tissues (including hyphaemas) in conjunction with ocular surgery. Diclofenac Devatis should be used with caution in patients with known haemostatic defects or who are receiving other medicinal products which may prolong bleeding time.

Patients should be advised not to wear contact lenses during treatment with Diclofenac Devatis.

4.5 Interactions with other medicinal products and other forms of interaction

Concomitant use of topical NSAIDs such as diclofenac and topical steroids in patients with significant pre-existing corneal inflammation may increase the risk of developing corneal complications, therefore caution should be used.

To prevent the active substances from being washed out when additional ophthalmic medication is used, an interval of at least 5 minutes between each application should be adhered to.

4.6 Fertility, pregnancy and lactation

Pregnancy
Inhibition of prostaglandin synthesis may adversely affect the pregnancy and/or the embryo/foetal development. Data from epidemiological studies suggest an increased risk of miscarriage and of cardiac malformation and gastroschisis after use of a prostaglandin synthesis inhibitor in early pregnancy. The absolute risk for cardiovascular malformation was increased from less than 1% up to approximately 1.5%.
The risk is believed to increase with dose and duration of therapy. In animals, administration of a prostaglandin synthesis inhibitor has shown to result in increased pre- and post-implantation loss and embryo-foetal lethality.
In addition, increased incidence of various malformations, including cardiovascular malformations, has been reported in animals given a prostaglandin synthesis inhibitor during organogenetic period.

During the third trimester of pregnancy, all prostaglandin synthesis inhibitors may expose the foetus to:
- cardiopulmonary toxicity (with premature closure of the ductus arteriosus and pulmonary hypertension);
- renal dysfunction, which can progress to renal failure with oligo-hydroamniosis;

the mother and the neonate, at the end of the pregnancy, to:
- possible prolongation of bleeding time, an anti-aggregating effect which may occur even at very low doses;
- inhibition of uterine contractions resulting in delayed or prolonged labour.

Despite the limited amount of data on the ocular use of diclofenac during pregnancy and due to the low systemic exposure, no adverse effects are expected from short-term use in low doses during the first and second trimesters.
Diclofenac should not be used during the third trimester unless strictly necessary.

Breast-feeding
Diclofenac is excreted in breast milk. However, at therapeutic doses of Diclofenac Devatis no effects on the suckling child are anticipated.

Fertility
Diclofenac sodium administered to male and female rats at 4 mg/kg/day (approximately 1000 times the human topical ophthalmic dose) did not affect fertility.

4.7 Effects on the ability to drive and use machines

Immediately after administration of Diclofenac Devatis, the ability to drive or use machines may be impaired due to blurred-vision.

4.8 Undesirable effects

Adverse reactions are ranked under heading of frequency, the most frequent first, using the following convention:
- 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)
- Not known (cannot be estimated from the available data)

The most frequently observed adverse reaction is a transient, mild to moderate eye irritation (10%) and/or blurred vision may occur immediately after administration of the eye drops.

Eye disorders

Common:	Eye irritation, blurred vision, conjunctivitis
Uncommon:	Eye pruritus, ocular hyperaemia, punctate keratitis
Rare:	Corneal defects, erythema, photosensitivity, intraocular pressure increased
Not known:	Eye pain

Immune system disorders

Rare:	Hypersensitivity

Punctate keratitis or corneal disorders have been observed, usually after frequent application.

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, ocular administration of diclofenac has been associated, in rare cases, with ulcerative keratitis, corneal thinning, punctuate keratitis, corneal epithelium defect and corneal oedema, which might become sight-threatening. Most patients were treated for a prolonged period of time.
Patients with evidence of corneal epithelial breakdown should immediately discontinue use of Diclofenac Devatis and should be monitored closely for corneal health (see section 4.4).

Allergic conditions have been reported for ocular reactions such as conjunctival hyperaemia, allergic conjunctivitis, eyelid erythema, oedema, and pruritus, and systemic hypersensitivity reactions such as urticaria, rash, eczema, erythema, pruritus, cough and rhinitis

In rare cases, dyspnoea and exacerbation of asthma cases have been reported.

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

In case of inadvertent oral intake only minor adverse reactions are to be expected due to the small amount of the active substance.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic Group: Anti-inflammatory agents, non-steroids,
ATC code: S01BC 03.

Diclofenac is a non-steroidal anti-inflammatory agent with analgesic properties. It is an inhibitor of the prostaglandin synthesis.
Clinical trials have shown that diclofenac, when administered preoperatively, inhibits miosis during cataract surgery and has an anti-inflammatory effect after cataract surgery.

5.2 Pharmacokinetic properties

In rabbits, peak concentrations of labelled diclofenac are demonstrated in the cornea and conjunctiva 30 minutes after application; elimination is fast and almost complete after 6 hours.

Penetration of diclofenac into the anterior chamber of the eye has been confirmed in humans. Following topical application in patients with cataracts, up to 570 ng/g diclofenac was detected in the aqueous humour 15 – 30 minutes after the final application.

Following ocular application of 0.1% diclofenac sodium eye drops, no detectable plasma levels of diclofenac were found in humans.

5.3 Preclinical safety data

Ocular instillation of diclofenac on various animal species revealed no specific sensitivity.

There are no more preclinical data considered relevant to clinical safety beyond data included in other sections of the SPC.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Macrogolglycerol ricinoleate
Boric acid (E284)
Trometamol
Water for injections

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years

After first opening of the sachet: 28 days, store the containers in the outer carton to protect from light.

After first opening of the single-dose container: the product must be used immediately and the remaining content discarded after use.

6.4 Special precautions for storage

Do not store above 25°C.
Store in the original package in order to protect from light and evaporation.
For storage conditions of the opened medicinal product, see section 6.3.

6.5 Nature and contents of container

0.3 ml transparent LDPE single-dose containers in PET aluminium/PE sachets containing 5 single dose containers each.

Pack-sizes: 10 x 0.3 ml, 20 x 0.3 ml, 30 x 0.3 ml, 40 x 0.3 ml, 50 x 0.3 ml, 60 x 0.3 ml and 120 x 0.3 ml single dose containers.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.

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

7. HOUDER VAN DE VERGUNNING VOOR HET IN DE HANDEL BRENGEN

Devatis GmbH
Spitalstr. 22
79539 Lörrach
Duitsland

8. NUMMER VAN DE VERGUNNING VOOR HET IN DE HANDEL BRENGEN

RVG 113364

9. DATUM VAN EERSTE VERLENING VAN DE VERGUNNING/VERLENGING VAN DE VERGUNNING

Datum van eerste verlening van de vergunning: 16 december 2014
Datum van laatste verlenging: 24 november 2019

10. DATUM VAN HERZIENING VAN DE TEKST

Laatste gedeeltelijke wijziging betreft rubrieken 4.4, 4.6, 4.8 en 9: 3 juli 2020