SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

NÉOMDEXSOL® 0,35 % / 0,1 %, eye drops solution.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1 ml contains:
3.5 mg neomycin (as sulphate)
1 mg dexamethasone phosphate (as dexamethasone sodium phosphate)
Excipients with known effect: benzalkonium chloride

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Eye drops solution
Clear colourless to pale yellow solution

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

Anti-inflammatory and anti-bacterial eye local treatment:
- Following ophthalmic surgery,
- Bacterial infections associated with inflammation caused by organisms sensitive to neomycin.

Consideration should be given to official guidance on the appropriate use of antibacterial agents.

4.2 Posology and method of administration

Posology
1 drops every hour at initiation of the treatment in severe and acute conditions; 3 to 6 times a day for other conditions, for 7 days in average.
Longer treatment or more frequent instillations may be prescribed under strict ophthalmological supervision.

Paediatric population
The use of this medicine should be avoided in infants.

Method of administration
To be applied locally, by eye (ocular) instillation in the inferior conjunctival fornix.

4.3 Contraindications

- Hypersensitivity to the active substances or to any excipients listed in section 6.1
- Herpetic epithelial dendritic keratitis
- Fungal or tuberculous eye infections
- Personal or family history of glaucoma
- Early stages of viral keratoconjunctivitis
- Purulent infections of eyelids and eyes caused by neomycin resistant germs.

4.4 Special warnings and precautions for use

Special warnings

Repeated and/or prolonged instillation of eye drops may result in a significant systemic leakage of the active ingredients.
Repeated and/or prolonged instillations may lead to ocular hypertonia in some patients and/or delayed healing.
Cushing's syndrome and/or inhibition of adrenal function associated with systemic absorption of ophthalmic dexamethasone may occur after continuous intensive or long-term treatment in predisposed patients, including children and patients treated with CYP3A4 inhibitors (including ritonavir and cobicistat). In this case, treatment should be stopped gradually.

Visual disorders

Visual disorders might occur during systemic or local corticosteroid therapy. In case of blurred vision or any other visual symptom during corticosteroid therapy, an ophthalmic examination is required notably to assess cataract, glaucoma, or rare damage as central serous chorioretinopathy.

athletes should be aware that this medicine contains an active substance which may induce a positive reaction to anti-doping tests.

Precautions for use

This eye drops solution is not intended for peri ocular or intra ocular injection.
If more than one ophthalmic medicinal product is being used, the medicines must be administered 15 minutes apart.
Sensitivity to topically applied neomycin sulphate may occur in some patients. If signs of serious reactions or hypersensitivity occur, the use of this medicine should be stopped.
In case of lack of improvement or in case of prolonged treatment, a medical supervision with microorganism's susceptibility studies is indicated to detect resistance and to eventually adapt the treatment.
This kind of association is, in general, contraindicated following a simple ablation of superficial corneal foreign body.
The use of corticosteroids in stroma herpes simplex required a close monitoring: the use of slit lamp examination is frequently required.
As with other corticosteroids ophthalmic preparations, prolonged use requires an ophthalmic monitoring of cornea, of intraocular pressure and of crystalline lens. Cases of thinning of the cornea and cases of cataract have been reported after prolonged use of local steroids.
Hereditary and degenerative eye diseases do not show a response to treatment with this medicine.
Wearing lenses should be avoided during treatment because of risk adsorption of the active ingredients and preservative.

Excipients with known effect:

NÉOMDEXSOL® 0,35%/ 0,1% contains benzalkonium chloride by.
Based on the limited data available, the adverse reaction profile in children is similar to the profile in adults. However, a stronger reaction to a given stimulus is generally observed in children than in adults. Irritation may affect compliance in children.
Benzalkonium chloride is known to cause eye irritation, symptoms of dry eye syndrome and may affect the tear film and corneal surface.
NÉOMDEXSOL 0.35% / 0.1%, eye drops solution should be used with caution in patients with dry eye and those at risk of corneal damage.
Patients should be monitored for prolonged use.

4.5 Interaction with other medicinal products and other forms of interaction

CYP3A4 inhibitors (including ritonavir and cobicistat) might decrease dexamethasone clearance causing an increase in the effects and inhibition of the adrenal function/Cushing syndrome. The combination should be avoided, except if the benefit is greater than the increased risk of systemic side effects of corticosteroids, in which case the patients should be monitored for the systemic effects of corticosteroids.

4.6 Pregnancy and breastfeeding

Pregnancy
It is preferable, as a precautionary measure not to use NEOMDEXSOL, eye drops in solution during pregnancy. Indeed, clinical and animal data with this combination by this route of use are insufficient. In clinical, foetal toxicity effects have been reported with systemic corticosteroids and aminoglycosides.

Breastfeeding
Breastfeeding is possible in case of short-term treatment (10 days). Breastfeeding is not recommended in case of prolonged treatment.

4.7 Effects on ability to drive and use machines

Not applicable.

4.8 Side effects

Possibility of transient local irritation: discomfort, lacrimation, burning, conjunctival hyperemia.
Risk of cutaneous-conjunctiva hypersensitivity reactions.
In case of prolonged use: corticosteroid-induced ocular hypertension, clouding of the lens, superficial keratitis.
In case of corneal or scleral ulceration, corticosteroids can delay healing and promote superinfection.
A few rare cases of corneal calcification have been reported in association with the use of phosphate-containing drops in some patients with severely damaged corneas.

Side effects from post marketing data (unknown frequency):
The following post marketing side effects were observed:
- Endocrinal disorders: Cushing syndrome, inhibition of the adrenal function (see section 4.4).
- Eye disorders: blurred vision (see section 4.4).

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 report any suspected adverse reactions by the national reporting system.

4.9 Overdose
No case of overdose has been reported. However, repeated instillation may lead to the systemic resorption of active ingredients, corticosteroid-induced ocular hypertension, clouding of the lens, superficial keratitis, and delay healing.
As with all ophthalmic preparations containing a corticosteroid, prolonged use requires particularly careful ophthalmological monitoring of the cornea, eye pressure and lens: cases of corneal thinning and cataracts have been reported after prolonged treatment with some local corticosteroids.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: ophthalmological; Corticosteroids and anti-infectives in combination. ATC code: S01CA01.
Dexamethasone is a steroidal anti-inflammatory drug.
Neomycin is an aminoglycoside bactericide antibiotic.

SPECTRUM OF ANTIBACTERIAL ACTIVITY OF NEOMYCIN
The prevalence of acquired resistance may vary depending on geography and time for some species. It is therefore useful to have information on the prevalence of local resistance, especially for the treatment of severe infections. These data can only provide guidance on the probabilities of susceptibility of a bacterial strain to this antibiotic.
When the variability in resistance prevalence is known for a bacterial species, it is shown in the table below:

Category	Frequency of acquired resistance in France (> 10 %) (extreme values)
SENSITIVE SPECIES	
Gram positive aerobic bacteria	50 – 75 %
Corynebacterium	
Listeria monocytogenes	20 – 25 %
Staphylococcus mehti-S	?
Gram negative aerobic bacteria	10 – 20 %
Acinetobacter (mainly Acinetobacter baumannii)	15 – 25 %
Branhamella catarrhalis	25 – 35 %
Campylobacter	10 – 15 %
Citrobacter freundii	10 – 20 %
Citrobacter koseri	20 – 50 %
Enterobacter aerogenes	?
Enterobacter cloacae	?
Escherichia coli	?
Haemophilus influenzae	?
Klebsiella	?
Morganella morganii	?
Proteus mirabilis	?
Proteus vulgaris	
Providencia rettgeri	
Salmonella	
Serratia	
Shigella	
Yersinia	

MODERATELY SENTIVE SPECIES (*in vitro* intermediate sensitivity) **Gram negative aerobic bacteria** *Pasteurella*	
RESISTANT SPECIES **Gram positive aerobic bacteria** **Enterococcus** *Nocardia asteroides* *Staphylococcus methi-R** *Streptococcus* **Gram negative aerobic bacteria** *Alcaligenes denitrificans* *Burkholderia* *Flavobacterium sp.* *Providencia stuartii* *Pseudomonas aeruginosa* *Stenotrophomonas maltophilia* **Anaerobic bacteria** Strict anaerobic bacteria **Others** *Chlamydia* Mycoplasma Rickettsia	

*The frequency of methicillin resistance is about 30 to 50 % of the whole staphylococcus and encountered mainly in hospital environment.

Note: This spectrum corresponds to that of systemic forms of antibiotics belonging to the aminoglycoside family. With local pharmaceutical presentations, the concentrations obtained *in situ* are much higher than plasma concentrations. Some doubts remain on the kinetics of *in situ* concentrations on local physico-chemical conditions that can modify the antibiotic activity and *in situ* product stability.

5.2 Pharmacokinetic properties
In topical use, neomycin poorly penetrates the cornea.

5.3 Preclinical safety data
None stated.

6. PHARMACEUTICAL PARTICULARS
6.1 List of excipients
Dibasic sodium phosphate (dihydrate); disodium edetate; benzalkonium chloride; mannitol; creatinine; sodium metabisulfite; glycerine; sodium sulfoxylate formaldehyde; sodium citrate; dihydrogen sodium phosphate, water for injections.

6.2 Incompatibilities
Not applicable

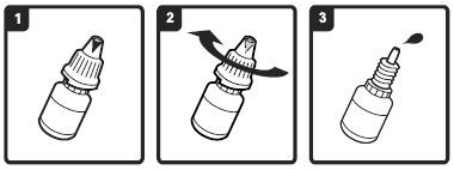
6.3 Shelf Life
Unopened: 2 years
Discard 1 month after first opening.

6.4 Special precautions for storage
Store at room temperature (below 30°C). Protect from light.
Discard 1 month after first opening.

6.5 Nature and contents of container
NÉOMDEXSOL® is available in 5 ml bottle made of transparent low-density polyethylene and with a plastic cap of white low-density polyethylene.

6.6 Special precautions for disposal and other handling of the product
No special requirements.

Bottle opening:



1. Place the cap, which has a spike, on the top of the vial.
2. Screw on the cap while pressing it down to pierce the vial.
3. Dispense the drops by applying gentle pressure to the vial. Replace the cap after each use.

7. CATEGORY OF DISTRIBUTION
☒ Prescription only medicine

Liste I

Prescription only medicine
List I

8. MARKETING AUTHORISATION HOLDER

Exphar s.a.
Zoning Industriel de Nivelles Sud, zone II
Avenue Thomas Edison 105
1402 Thines, Belgium

9. MANUFACTURER

Ahlcon Parenterals (India) Ltd.
SP 917-918, Phase III, Industrial Area
Bhiwadi, 301019 - District Alwar (Rajasthan)-India

10. DATE OF THE REVISION OF THE TEXT
October 2022.