For the use only of Registered Medical Practitioners or a Hospital or a Laboratory

BETNESOL-N

1. GENERIC NAME

Betamethasone Sodium Phosphate and Neomycin Sulphate Eye/Ear Drops

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Contains:

Betamethasone Sodium Phosphate IP	0.1% w/v
Neomycin Sulphate IP	0.5% w/v
Thiomersal IP (Preservative)	0.005% w/v
(Appropriate overages added)	

List of Excipients

Disodium Edetate, Sodium Formate, Thiomersal, Sodium Hydroxide, Water for Injection.

3. DOSAGE FORM AND STRENGTH

Solution.

For information on strength(s) refer *2. Qualitative and Quantitative Composition* above.

4. CLINICAL PARTICULARS

4.1 Therapeutic Indication

Eyes

Non-infected steroid responsive inflammatory conditions e.g.

- Uveitis.
- Marginal keratitis.
- Allergic conjunctivitis
- Blepharitis.
- Episcleritis.
- where prophylaxis against secondary bacterial infection is desired.

Ears

Otitis externa and other steroid responsive inflammatory conditions where bacterial infection is present or suspected (see *4.3 Contraindications*).

4.2 Posology and Method of Administration

Treatment should not be continued for more than seven days without medical supervision.

Populations

Adults

Eyes

1 or 2 drops instilled into the eye every 1 or 2 hours until signs of improvement are apparent, when the frequency may be reduced.

Ears

2 or 3 drops instilled into the ear every 2 or 3 hours until signs of improvement are apparent, when the frequency can be reduced.

Children

BETNESOL-N is suitable for use in children (2 years and over) at the same dose as adults. A possibility of increased absorption exists in very young children, thus *BETNESOL-N* is not recommended for use in neonates and infants (less than 2 years) (see *4.3 Contraindications* and *4.4 Special Warnings and Precautions for Use*).

Elderly

BETNESOL-N may be used in the elderly. Caution should be exercised in cases where a decrease in renal function exists and significant systemic absorption of neomycin sulphate may occur (see *4.4 Special Warnings and Precautions for Use*).

Renal impairment

Dosage should be reduced in patients with reduced renal function (see *4.4 Special Warnings and Precautions for Use*)

4.3 Contraindications

- Viral, fungal, tuberculous or purulent conditions.

- Hypersensitivity to the preparation.

Eye Drops

- Use in the eye is contraindicated if glaucoma is present or where herpetic keratitis (e.g. dendritic ulcer) is considered a possibility. Inadvertent use of topical steroids in the latter condition can lead to extension of the ulcer and marked visual deterioration.

Ear Drops

- Because of the risk of ototoxicity, preparations containing neomycin should not be used until an intact tympanic membrane has been visualised.

- Due to the known ototoxic and nephrotoxic potential of neomycin sulphate, the use of *BETNESOL-N* in large quantities or on large areas for prolonged periods of time is not recommended in circumstances where significant systemic absorption may occur.

- A possibility of increased absorption exists in very young children, thus *BETNESOL-N* is not recommended for use in neonates and infants (up to 2 years). In neonates and infants, absorption by immature skin may be enhanced, and renal function may be immature.

4.4 Special Warnings and Precautions for Use

Eye drops

Steroids should not be administered to 'red eyes' until a definitive diagnosis is made.

Treatment with steroid preparations should not be repeated or prolonged without regular review to exclude raised intra-ocular pressure or unsuspected infections.

All formulations

Long-term continuous topical therapy should be avoided where possible, particularly in children, as adrenal suppression can occur even without occlusion.

Visual disturbance has been reported by patients using systemic and /or topical corticosteroids. If a patient has blurred vision or other visual disturbances, consider evaluation of possible causes which may include central serous chorioretinopathy.
Pseudomembranous colitis has been reported with the use of antibiotics and may range in severity from mild to life-threatening. Therefore, it is important to consider its diagnosis in patients who develop diarrhoea during or after antibiotic use. If prolonged or significant diarrhoea occurs or the patient experiences abdominal cramps, treatment should be discontinued immediately and the patient investigated further.

The unnecessary topical use of neomycin containing products should be avoided in order to minimise occurrence of neomycin resistant organisms (and organisms cross-resistant to other aminoglycosides).

Following significant systemic absorption, aminoglycosides such as neomycin can cause irreversible ototoxicity; also, neomycin has nephrotoxic potential.

In renal impairment the plasma clearance of neomycin is reduced (see *4.2 Posology and Method of Administration*).

4.5 Drug Interactions

Following significant systemic absorption, neomycin sulphate can intensify and prolong the respiratory depressant effects of neuromuscular blocking agents.

4.6 Use in Special Populations

Pregnancy and Lactation

There is little information to demonstrate the possible effect of topically applied neomycin in pregnancy and lactation. However, neomycin present in maternal blood can cross the placenta and may give rise to a theoretical risk of foetal toxicity, thus use of *BETNESOL-N* is not recommended in pregnancy or lactation.

4.7 Effects on Ability to Drive and Use Machines

None identified.

4.8 Undesirable Effects

Eye Drops

Eye drops containing corticosteroids cause a serious rise in intra-ocular pressure in a small percentage of the population, including most of those with a family history of glaucoma. A milder rise may be experienced by a larger proportion of subjects if treatment is continued for longer than a few weeks.

Thinning of the cornea leading to perforation has occurred with use of topical corticosteroids.

Cataract is reported to have occurred after unduly prolonged treatment of eye conditions with topical corticosteroids.

All formulations

Acute sensitisation to neomycin is a rare event.

4.9 Overdose

Acute overdosage is very unlikely to occur, however, in the case of chronic overdose or misuse the features of hypercortisolism may appear and in this situation topical steroids should be discontinued gradually. However, because of the risk of acute adrenal suppression this should be done under medical supervision.

Also, consideration should be given to significant systemic absorption of neomycin sulphate (*see 4.4 Special Warnings and Precautions for Use*). If this is suspected, use of the product should be stopped and the patient's general status, hearing acuity, renal and neuromuscular functions should be monitored.

Blood levels of neomycin sulphate should also be determined. Haemodialysis may reduce the serum level of neomycin sulphate.

5. PHARMACOLOGICAL PROPERTIES

5.1 Mechanism of Action

Betamethasone

Corticosteroids exhibit anti-inflammatory, antipruritic, and vasoconstrictive properties. At the cellular level, corticosteroids induce peptides called lipocortins. Lipocortins antagonize phospholipase A2, an enzyme which causes the breakdown of leukocyte lysosomal membranes to release arachidonic acid. This action decreases the subsequent formation and release of endogenous inflammatory mediators including prostaglandins, kinins, histamine, liposomal enzymes and the complement system.

Early anti-inflammatory effects of topical corticosteroids include the inhibition of macrophage and leukocyte movement and activity in the inflamed area by reversing vascular dilation and permeability. Later inflammatory processes such as capillary production, collagen deposition, keloid (scar) formation also are inhibited by corticosteroids. Clinically, these actions correspond to decreased edema, erythema, pruritus, plaque formation and scaling of the affected skin.

Neomycin sulphate

Neomycin is bactericidal in action. Similar to other aminoglycosides, it inhibits bacterial protein synthesis through irreversible binding to the 30 S ribosomal subunit of susceptible bacteria. Neomycin is actively transported into the bacterial cell where it binds to receptors present on the 30 S ribosomal subunit. This binding interferes with the initiation complex between the messenger RNA (mRNA) and the subunit. As a result, abnormal, nonfunctional proteins are formed due to misreading of the bacterial DNA. Eventually, susceptible bacteria die because of the lack of functional proteins.

5.2 Pharmacodynamic Properties

See above.

5.3 Pharmacokinetic Properties

Betamethasone

No relevant text.

Neomycin sulphate

No relevant text.

6. NONCLINICAL PROPERTIES

No relevant text.

7. DESCRIPTION

Solution

Contains:

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List of Excipients

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8. PHARMACEUTICAL PARTICULARS

8.1 Incompatibilities

There are no relevant data available.

8.2 Shelf Life

The expiry date is indicated on the label and packaging.

The contents should not be used more than four weeks after first opening the bottle.

8.3 Packaging Information

Vial in a carton with a dropper.

8.4 Storage and Handling Instructions

Store at temperature not exceeding 30º C, protected from direct sunlight.

Use the solution within one month after opening the container.

Keep out of reach of children.

Do not dilute.

For external use only. Not for Injection.

Do not touch dropper tip to any surface since this may contaminate the solution.

9. PATIENT COUNSELLING INFORMATION

Registered Medical Practitioners may counsel their patients (and/or patients' caregiver as applicable) about the special warnings and precautions for use, drug interactions, undesirable effects, and any relevant contraindications of *BETNESOL-N*. Patients (and/or patients' caregiver) may also be informed about posology, method of administration and storage/handling information as applicable.

10. DETAILS OF MANUFACTURER

The Manufacturing Site details are mentioned on the label and packaging.

For further information please contact:
GlaxoSmithKline Pharmaceuticals Limited.
Registered Office:
Dr. Annie Besant Road, Worli
Mumbai 400 030, India.

11. DETAILS OF PERMISSION OR LICENCE NUMBER WITH DATE

Manufacturing License number is indicated on the label and packaging.

12. DATE OF REVISION

25-AUG-2023

Version: BET-NEE/PI/IN/2023/01

Adapted from: Betamethasone sodium phosphate-Neomycin sulphate GDS v 07 dated 03 April 2018.