## 1. Name of the medicinal product

Betamethasone Sodium Phosphate and Neomycin sulphate eye/ear & nose drops (X BETA N Eye/Ear & Nose drops)

## 2. Qualitative and quantitative composition

Betamethasone Sodium Phosphate B.P 0.10% w/v.

Neomycin Sulphate equivalent B.P 0.50% w/v.

Excipient(s) with known effect:

None

For the full list of excipients, see section 6.1.

## 3. Pharmaceutical form

Ear/Eye/Nose Drops, Solution

A colourless to pale yellow solution.

## 4. Clinical particulars

### 4.1 Therapeutic indications

Eye

Short-term treatment of steroid responsive inflammatory conditions of the eye when prophylactic antibiotic treatment is also required, after excluding the presence of viral and fungal disease.

Ear

Otitis externa or other steroid responsive conditions where prophylactic antibiotic treatment is also required.

Nose

Steroid responsive inflammatory conditions where prophylactic antibiotic treatment is also required.

### 4.2 Therapeutic indications

The frequency of dosing depends on the clinical response. If there is no clinical response within 7 days of treatment, the drops should be discontinued.

Treatment should be the lowest effective dose for the shortest possible time. Normally, X BETA N Drops should not be given for more than 7 days, unless under expert supervision. After more prolonged treatment (over 6 to 8 weeks), the drops should be withdrawn slowly to avoid relapse.

Eyes

1 or 2 drops applied to each affected eye up to six times daily depending on clinical response.

Ears

2 or 3 drops instilled into the ear three or four times daily.

Nose

2 or 3 drops instilled into each nostril two or three times daily.

## 4.3 Contraindications

Viral, fungal, tuberculous or purulent conditions of the eye. Fungal infections of the nose or ear. Use is contra-indicated if glaucoma is present or herpetic keratitis (e.g. dendritic ulcer) is considered a possibility. Use of topical steroids in the latter condition can lead to an extension of the ulcer and marked visual deterioration.

Otitis externa should not be treated when the eardrum is perforated because of the risk of ototoxicity.

Corticosteroids should not be used in patients with a perforated tympanic membrane.

Hypersensitivity to any component of the preparation

## 4.4 Special warnings and special precautions for use

A patient information leaflet should be supplied with this product.

Topical corticosteroids should never be given for an undiagnosed red eye as inappropriate use is potentially blinding.

Treatment with corticosteroid/antibiotic combinations should not be continued for more than 7 days in the absence of any clinical improvement, since prolonged use may lead to occult extension of infection due to the masking effect of the steroid. Prolonged use may also lead to skin sensitisation and the emergence of resistant organisms.

Ophthalmological treatment with corticosteroid preparations should not be repeated or prolonged without regular review to exclude raised intraocular pressure, cataract formation or unsuspected infections.

Aminoglycoside antibiotics may cause irreversible, partial or total deafness when given systemically or when applied topically to open wounds or damaged skin. This effect is dose related and is enhanced by renal or hepatic impairment. Although this effect has not been reported following topical ocular use, the possibility should be considered when high dose topical treatment is given to small children or infants.

There have been observed cases of an increased risk of ototoxicity with aminoglycosides administered to patients with mitochondrial mutations, particularly the m.1555A>G mutation, including cases where the patient's aminoglycoside serum levels were within the recommended range. Some cases were associated with a maternal history of deafness and/or mitochondrial mutation. While no cases were identified with neomycin, based on a shared mechanism of action there is the potential for a similar effect with neomycin. These mitochondrial mutations are rare, and the penetrance of this observed effect is unknown.

Nasal administration of corticosteroids is not advised if an untreated nasal infection is present or if the patient has pulmonary tuberculosis or following nasal surgery (until healing has occurred).

Systemic effects of nasal corticosteroids may occur, particularly at high doses prescribed for prolonged periods. These effects are much less likely to occur than with oral corticosteroids and may vary in individual patients and between different corticosteroid preparations. Potential systemic effects may include Cushing's syndrome, Cushingoid features, adrenal suppression, growth retardation in children and adolescents, cataract, glaucoma and more rarely, a range of psychological or behavioural effects including psychomotor hyperactivity, sleep disorders, anxiety, depression or aggression (particularly in children).

Visual disturbance may be reported with systemic and topical corticosteroid use. If a patient presents with symptoms such as blurred vision or other visual disturbances, the patient should be considered for referral to an ophthalmologist for evaluation of possible causes which may include cataract, glaucoma or rare diseases such as central serous chorioretinopathy (CSCR) which have been reported after use of systemic and topical corticosteroids.

Excipients with specified warnings

Not applicable

**4.5 Interaction with other medicinal products and other forms of interaction**

Co-treatment with CYP3A inhibitors, including cobicistat-containing products, is expected to increase the risk of systemic side-effects. The combination should be avoided unless the benefit outweighs the increased risk of systemic corticosteroid side-effects, in which case patients should be monitored for systemic corticosteroid side-effects.

**4.6 Fertility, pregnancy and lactation**

Safety for use in pregnancy and lactation has not been established. There is inadequate evidence of safety in human pregnancy. Topical administration of corticosteroids to pregnant animals can cause abnormalities of foetal development including cleft palate and intrauterine growth retardation. There may therefore be a very small risk of such effects in the human foetus.

There is a risk of foetal ototoxicity if aminoglycoside antibiotic preparations are administered during pregnancy.

**4.7 Effects on ability to drive and use machines**

May cause transient blurring of vision on instillation. Patients should be warned not to drive or operate hazardous machinery unless vision is clear.

## 4.8 Undesirable effects

Hypersensitivity reactions, usually of the delayed type, may occur leading to irritation, burning, stinging, itching and dermatitis.

Topical corticosteroid use may result in corneal ulceration, increased intraocular pressure leading to optic nerve damage, reduced visual acuity and visual field defects.

Intensive or prolonged use of topical corticosteroids may lead to formation of posterior subcapsular cataracts.

In those diseases causing thinning of the cornea or sclera, corticosteroid therapy may result in thinning of the globe leading to perforation.

Mydriasis, ptosis, epithelial punctate keratitis and glaucoma have also been reported following ophthalmic use of corticosteroids.

Cases of corneal calcification have been reported very rarely in association with the use of phosphate containing eye drops in some patients with significantly damaged corneas.

Following nasal administration, the most common effects are nasal irritation and dryness, although sneezing, headache, light headedness, urticaria, nausea, epistaxis, rebound congestion, bronchial asthma, perforation of the nasal septum, ulceration of the nasal septum, anosmia, parosmia and disturbance to sense of taste have also been reported.

Systemic effects of nasal corticosteroids may occur, particularly at high doses prescribed for prolonged periods. Growth retardation has been reported in children receiving nasal corticosteroids at licensed doses.

It is recommended that the height of children receiving prolonged treatment with nasal corticosteroids is regularly monitored. If growth is slowed, therapy should be reviewed with the aim of reducing the dose of nasal corticosteroid, if possible, to the lowest dose at which effective control of symptoms is maintained. In addition, consideration should also be given to referring the patient to a paediatric specialist.

Vision, blurred (see also 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 are asked to report any suspected adverse reactions.

### 4.9 Overdose

Long-term intensive topical use may lead to systemic effects.

Oral ingestion of the contents of one bottle (up to 10ml) is unlikely to lead to any serious adverse effects.

Treatment with higher than recommended doses may result in clinically significant adrenal suppression. If there is evidence of higher than recommended doses being used then additional systemic corticosteroid cover should be considered during periods of stress or elective surgery.

## 5. Pharmacological Properties

### 5.1 Pharmacodynamic properties

**Pharmacotherapeutic group**: ophthalmic steroid-antibiotic combined preparations.

**ATC code**: **S03C A; corticosteroids and ant infectives in combination**

**S03C A06; betamethasone and anti-infectives**

Betamethasone has topical corticosteroid activity. The presence of neomycin should prevent the development of bacterial infection.

### 5.2 Pharmacokinetic properties

Pharmaceutical class: Corticosteroids and anti-infectives

### 5.3 Preclinical safety data

None stated.

## 6. Pharmaceutical particulars

### 6.1 List of excipients

- Disodium edetate
- Thiomersal
- Sodium Chloride
- Water for injections

### 6.2 Incompatibilities

Not applicable.

### 6.3 Shelf life

Unopened: 30 months

Use within 28 days of first opening

Discard four weeks of first opening

### 6.4 Special precautions for storage

Store at a temperature not exceeding 25°C. Avoid freezing. Always replace the bottle back in the carton after use to protect its contents from light. The sterility of the drops is assured until the cap seal is broken

### 6.5 Nature and contents of container

Low density polyethylene dropper bottles and a white screw cap in pack sizes of 10mL.

### 6.6 Special precautions for disposal and other handling

No special requirements.

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

## 7. Marketing authorization holder

Abacus Parenteral Drugs Limited
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Email: apdl@abacuspharma.com
Website: www.abacuspharma.com

## 8. Marketing authorization number(s)

NDA/MAL/HDP/4030

## 9. Date of first authorization/renewal of the authorization

First Authorisation: 10/06/2011

Renewal of authorization: 2017

## 10. Date of revision of the text