**SCHEDULING STATUS**

**S4**

## 1. NAME OF THE MEDICINE

**BETNESOL EYE, EAR AND NOSE DROPS 1 mg/ml solution for drops**

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 1 ml of BETNESOL EYE, EAR AND NOSE DROPS contains 1 mg of betamethasone sodium phosphate in a sterile stabilised solution

Preservative: Benzalkonium chloride 0,02 % m/v

For full list of excipients, see section 6.1.

## 3. PHARMACEUTICAL FORM

Solution

BETNESOL EYE, EAR AND NOSE DROPS is a colourless to slightly yellow, clear solution, free from particles.

## 4. CLINICAL PARTICULARS

### 4.1. Therapeutic indications

Eye conditions: Treatment of non-infected inflammatory conditions such as non-specific keratitis, conjunctival allergies and acute or chronic uveitis.

Ear conditions: Treatment of inflammatory conditions of the ear such as otitis externa.

Nose conditions: Treatment of hayfever, vasomotor and non-seasonal allergic rhinitis.

### 4.2. Posology and method of administration

**Posology**

EYE: One or two drops to be instilled into the eye every one or two hours until control is achieved, when the frequency may be reduced.

EAR: Two to three drops to be instilled into the ear every two or three hours until control is achieved, when the frequency may be reduced.

NOSE: Two or three drops to be instilled into each nostril two or three times daily.

Short courses at high doses for emergencies appear to cause fewer side effects than prolonged courses with lower doses.

Because of the possibility of inducing corneal abscess, fungal keratopathy or glaucoma, the patient should be referred to an ophthalmologist if the eye has not responded within 48 hours (see section 4.4 and 4.8).

**Paediatric population**

In infants, long-term continuous topical therapy should be avoided where possible, as adrenal suppression (see section 4.8) can occur even without occlusion. The least potent corticosteroid which will control the disease should be selected

## 4.3. Contraindications

- BETNESOL EYE, EAR AND NOSE DROPS should not be used for the treatment of ulcerative conditions, nor of rosacea, and should not be used indiscriminately for pruritus.
- BETNESOL EYE, EAR AND NOSE DROPS is contraindicated in the treatment of herpes simplex, vaccinia or varicella.
- Patients with a perforated tympanic membrane.
- Children receiving high doses of corticosteroids included in BETNESOL EYE, EAR AND NOSE DROPS are at special risk of diseases, such as chickenpox, but

vaccination with organisms is contraindicated since infections may be induced (see section 4.5).

## 4.4. Special warnings and precautions for use

Because of the possibility of inducing corneal abscess, fungal keratopathy or glaucoma, the patient should be referred to an ophthalmologist if the eye has not responded within 48 hours (see section 4.2 and 4.8).

High doses of corticosteroids administered during pregnancy may cause foetal or neonatal adrenal suppression (see section 4.6).

BETNESOL EYE, EAR AND NOSE DROPS should be used with caution in the presence of heart failure, recent myocardial infarction, or hypertension, in patients with diabetes mellitus, epilepsy, glaucoma, hypothyroidism, hepatic failure, osteoporosis, peptic ulceration, psychoses or severe affective disorders, and renal impairment.

The elderly may too be at greater risk from adverse effects.

Patients should be examined regularly during prolonged courses of treatment.

Cataract is reported to have occurred after unduly prolonged treatment of eye conditions with ophthalmic corticosteroids such as BETNESOL EYE, EAR AND NOSE DROPS (see section 4.8)

Visual disturbance have been reported with the use of BETNESOL EYE, EAR AND NOSE DROPS. If a patient presents with symptoms such as blurred vision or other visual disturbances, the patient should be referred to an ophthalmologist for evaluation of possible causes such as cataract, glaucoma or central serous chorioretinopathy (CSCR).

Treatment should be the lowest effective dose for the shortest possible time.

After more prolonged treatment (over 6 to 8 weeks), the drops should be withdrawn slowly to avoid relapse.

Large doses of corticosteroid, particularly if prescribed for prolonged periods may produce:

- Cushingoid symptoms typical of hyperactivity of the adrenal cortex, with moon-face, sometimes with hirsutism, buffalo hump, flushing, increased bruising, ecchymoses, striae and acne (see section 4.8).
- Adrenal suppression,
- Growth retardation in children and adolescents
- Cataract and glaucoma
- Psychological or behavioural effects including psychomotor hyperactivity, sleep disorders, anxiety, depression or aggression - particularly in children. These psychological disorders occurvery rarely.
- An altered tissue repair and immune function response of the body to which permits the spread of infections, frequently in forms such as disseminated parasitic infections. This effect may also occur if the patient is receiving other immunosuppressants such as cytotoxic medicines or if they are already debilitated. (see section 4.5 and 4.8)

High dose corticosteroid doses; even if given for short courses, may cause corticosteroid-induced avascular necrosis of bone. The incidence of this uncommon but disabling complication of therapy varies in patients with different disease states like alcoholism, and patients with connective tissue disease (especially systemic lupus erythematosus) may have increased susceptibility to this complication developing (see section 4.5 and 4.8)

- The use of pharmacological doses of BETNESOL EYE, EAR AND NOSE DROPS suppresses the endogenous secretion of corticotropin by the anterior pituitary, with the result that the adrenal cortex becomes atrophied.

This adrenal atrophy occurs due to the negative feedback effects of corticosteroids such as BETNESOL EYE, EAR AND NOSE DROPS on the hypothalamic-pituitary-adrenal (HPA) axis and can occur after just 7 days' treatment (see section 4.8).

Sudden withdrawal or reduction in dosage, or an increase in the requirements of BETNESOL EYE, EAR AND NOSE DROPS with the stress of infection or accidental or surgical trauma, may precipitate acute adrenal insufficiency.

Duration of treatment, dosage and individual liability to suppression are important factors in determining suppression of the pituitary-adrenal response to stress on cessation of BETNESOL EYE, EAR AND NOSE DROPS treatment.

Patients vary considerably in degree and duration of adrenal suppression following a given course of corticosteroid, but adrenal atrophy may persist for months or years, and withdrawal should be gradual in those who have been treated for any length of time (see section 4.8)

- Other effects that may occur during withdrawal or change of BETNESOL EYE, EAR AND NOSE DROPS include fever, myalgia, arthralgia, weight loss, benign intracranial hypertension with headache and vomiting, and papilloedema caused by cerebral oedema.

Following short courses at moderate doses it may be appropriate to withdraw BETNESOL EYE, EAR AND NOSE DROPS without tapering the dose. However, after high-dose or prolonged therapy, withdrawal should be gradual, the rate depending upon the individual patient's response, the dosage, the disease being treated, and the duration of therapy.

**Warnings related to benzalkonium chloride in the formulation:**

- BETNESOL EYE, EAR AND NOSE DROPS contains benzalkonium chloride as a preservative and therefore should not be used to treat patients who wear soft contact lenses (see section 4.3).
- Caution should be exercised in the use of benzalkonium chloride preserved topical medication over an extended period in patients with extensive ocular surface disease.
- Benzalkonium chloride may also cause eye irritation, especially in patients with dry eyes or disorders of the cornea. It may also cause irritation or swelling inside the nose,

especially if used for a prolonged periods (see section 4.8)

As the possibility of adverse effects on the corneal permeability and the danger of disruption of the corneal epithelium with prolonged or repeated usage of benzalkonium chloride preserved ophthalmological preparations cannot be excluded, regular ophthalmological examination is required (see section 4.8)

**Paediatric population**

Children may be at increased risk of some adverse effects; in addition, BETNESOL EYE, EAR AND NOSE DROPS may cause growth retardation, and prolonged administration is rarely justified (see section 4.2, 4.3 and 4.8).

Although the precise mechanism is uncertain, growth retardation may follow the administration of even relatively small doses of corticosteroids in children 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 (see section 4.8)

## 4.5. Interaction with other medicines and other forms of interaction

Co-treatment with CYP3A inhibitors, including the oral contraceptive female hormones (progesterone and oestrogen) and antivirals like ritonavir and cobicistat 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.

Concurrent use of barbiturates, carbamazepine, phenytoin, primidone, or rifampicin may enhance the metabolism and reduce the effects of systemic corticosteroids included in BETNESOL EYE, EAR AND NOSE DROPS.

Use with potassium-depleting diuretics, such as thiazides and furosemide, may cause

excessive potassium loss. There is also an increased risk of hypokalaemia with concurrent Amphotericin B or bronchodilator therapy with xanthines or beta2 agonists.

There may be an increased incidence of gastrointestinal bleeding and ulceration when given with nonsteroidal anti-inflammatory medicines. Response to anticoagulants may be altered by BETNESOL EYE, EAR AND NOSE DROPS and requirements of antidiabetic and antihypertensive medicines may be increased.

BETNESOL EYE, EAR AND NOSE DROPS may decrease serum concentrations of salicylates and may decrease the effect of antimuscarinics in myasthenia gravis.

Interactions are possible with, neuromuscular blockers.

BETNESOL EYE, EAR AND NOSE DROPS contains benzalkonium chloride as a preservative and therefore, should not be used to treat patients who wear soft contact lenses (see section 4.3 and 4.4).

In patients receiving other immunosuppressants such as cytotoxic medicines ,an altered tissue repair and immune function response may occur which permits the spread of infections such as disseminated parasitic infections (see section 4.4 and 4.8).

**Special populations**

Corticosteroid-induced avascular necrosis of bone is an uncommon but disabling complication of therapy with BETNESOL EYE, EAR AND NOSE DROPS. The incidence may vary in patients with different disease states, alcoholics, and patients with connective tissue disease (especially systemic lupus erythematosus) may have increased susceptibility. There may be a relationship with the dose; such that even short courses of high doses may be associated with its development. (see section 4.4 and 4.8).

In diseases causing thinning of the cornea, perforation has occurred with use of ophthalmic corticosteroids (see section 4.8)

**Paediatric population**

Children receiving high doses of the corticosteroid included in BETNESOL EYE, EAR AND

NOSE DROPS are at special risk of diseases, such as chickenpox, however, vaccination with live-attenuated organisms is contraindicated since infections may be induced (see section 4.3).

## 4.6. Fertility, pregnancy and lactation

When high doses of the corticosteroid included in BETNESOL EYE, EAR AND NOSE DROPS is administered during pregnancy, it may cause foetal or neonatal adrenal suppression (see section 4.3)

The corticosteroid included in BETNESOL EYE, EAR AND NOSE DROPS has been shown to be teratogenic in animals following dermal application. As these agents are absorbed percutaneously, teratogenicity following topical application can thus not be excluded (see section 4.3).

**Pregnancy**

BETNESOL EYE, EAR AND NOSE DROPS should not be used during pregnancy.

**Breastfeeding**

Safety for use in lactation has not been established

**Fertility**

No data are available.

## 4.7. Effects on ability to drive and use machines

BETNESOL EYE, EAR AND NOSE DROPS has a moderate influence on the 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

a) Summary of the safety profile

Most topically applied corticosteroids may, under certain circumstances, be absorbed in sufficient amounts to produce systemic effects.

BETNESOL EYE, EAR AND NOSE DROPS has no effects on sodium and water retention.

Increased severity of varicella with a possible fatal outcome in non-immune patients receiving systemic corticosteroid therapy has been reported.

Adverse effects occur, in general, fairly equally with all systemic corticosteroid preparations and their incidence rises steeply if dosage increases occur.

Adverse effects should be treated symptomatically, with the corticosteroid dosage reduced or slowly withdrawn where possible.

b) Tabulated list of adverse reactions

| | | | |
|---|---|---|---|
| **Musculoskeletal and connective tissue disorders** | - | | Avascular necrosis of bone (see section 4.4 and 4.5), muscle wasting, osteoporosis. |
| **Reproductive system and breast disorders** | | | Menstrual irregularities, amenorrhoea |
| **General disorders and administrative site conditions** | | Ulceration or perforation of the nasal septum | Dryness and irritation of the nasal septum, epistaxis, smell and taste disturbances. sneezing, headache, lightheadedness, rebound congestion, perforation of the nasal septum, ulceration of the nasal septum, Hypersensitivity that results in |

| | | | |
|---|---|---|---|
| | | | irritation, burning, stinging, itching and dermatitis. |

c) Description of selected adverse reactions

Eye preparations such as BETNESOL EYE, EAR AND NOSE DROPS can cause a serious rise in intra-ocular pressure in a small percentage of the population. A milder rise in ocular tension may be experienced by a larger proportion of subjects if treatment is continued for no longer than a few weeks.

The benzalkonium chloride included as a preservative in BETNESOL EYE, EAR AND NOSE DROPS may also cause eye irritation, especially in patients with dry eyes or disorders of the cornea. It may cause irritation or swelling inside the nose, especially if used for a long time (see section 4.4).

d) Paediatric population

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 (see section 4.2 and 4.4)

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare providers are asked to report any suspected adverse reactions to SAHPRA via the “6.04 Adverse Drug Reactions Reporting Form”, found online under SAHPRA’s publications:

https://www.sahpra.org.za/Publications/Index/8.

Reporting can also be done directly to Adcock Ingram Limited at:

Adcock Ingram Limited:

E-mail: Adcock.aereports@adcock.com

Tel: 011 635 0134

### 4.9. Overdose

The quantity of betamethasone sodium phosphate present is such that systemic absorption is unlikely to occur to any significant extent. In these circumstances, overdosage is unlikely, although appropriate care should be taken as noted under Undesirable effects and Special warnings and precautions for use (see sections 4.8 and 4.4).

## 5. PHARMACOLOGICAL PROPERTIES

BETNESOL EYE, EAR AND NOSE DROPS contain the water-soluble corticosteroid betamethasone sodium phosphate, and have the advantage of containing no steroid particles to cause irritation. This is of particular value in ophthalmic work

### 5.1. Pharmacodynamic properties

Category and Class: A 15.2 Ophthalmic preparations with corticosteroids

Pharmacotherapeutic group: Ophthalmological and otological preparations - Corticosteroids
ATC code: S03BA

### 5.2. Pharmacokinetic properties

Not applicable

## 6. PHARMACEUTICAL PARTICULARS

### 6.1 List of excipients

Benzalkonium chloride, disodium edetate, sodium chloride, water for injection

### 6.2 Incompatibilities

Not applicable.

### 6.3 Shelf life

24 months if kept in the original packaging and stored at or below 25 °C.
The shelf life after opening is 28 days.

### 6.4 Special precautions for storage

Store at or below 25 °C
Protect from light.
Avoid freezing.
Eye drops should be discarded within four weeks of first opening the container.
Keep in original packaging until required for use

### 6.5 Nature and contents of container

5 ml is packed into an opaque low density polyethylene bottle with an opaque low density polyethylene drop applicator, and sealed with a white polypropylene tamper evident cap. The sealed bottles are packed into unit cartons.

### 6.6 Special precautions for disposal and other handling

No special requirements.

## 7. HOLDER OF CERTIFICATE OF REGISTRATION

**Adcock Ingram Limited**
1 New Road,
Erand Gardens,
Midrand,1685
Customer Care: 0860 ADCOCK/ 232625

## 8. REGISTRATION NUMBER

H1257 (Act 101/1965)

## 9. DATE OF FIRST AUTHORISATION

Old medicine

## 10. DATE OF REVISION OF TEXT

09 September 2022