1.3Product Information

1.3.1 SPC, Labeling and Package Leaflet

SPC-Summary of Product Characteristics

Route of Administration: For Opthalmic use only.

SPC-Summary of Product Characteristics

1. Name of the Medicinal Product

Dexamethasone Sodium Phosphate Ophthalmic Solution USP

2. Qualitative and Quantitative Composition

Each ml contains:

Dexamethasone sodium phosphate USP

Eq. to Dexamethasone Phosphate 0.1% W/V

Benzalkonium Chloride solution BP 0.02 % W/V

(As Preservative)

Sterile Aqueous Base Q.S.

3. Pharmaceutical Form

Eye Drops

A clear, colourless solution in plastic bottle.

4. Clinical Particulars

4.1 Therapeutic Indications

Non-infected, steroid responsive, inflammatory conditions of the eye.

4.2 Posology and Method of Administration

Posology

Adults and the elderly

One or two drops should be applied topically to the eye up to six times a day. *Note:* In severe conditions the treatment may be initiated with 1 or 2 drops every hour, the dosage should then be gradually reduced as the inflammation subsides.

Paediatric population

At the discretion of the physician.

4.3 Contraindications

Use is contra-indicated in herpes simplex and other viral diseases of the cornea and conjunctiva, fungal disease, ocular tuberculosis, untreated purulent infections and hypersensitivity to any component of the preparation.

In children, long-term, continuous corticosteroid therapy should be avoided due to possible adrenal suppression.

4.4 Special Warnings and Precautions for use

Care should be taken to ensure that the eye is not infected before Dexamethasone Sodium Phosphate Eye Drops BP Dexamethasone sodium phosphate 0.1% w/v Eye Drops, solution is used.

These drops should be used cautiously in patients with glaucoma and should be considered carefully in patients with a family history of this disease.

This medicinal product contains phosphates which may lead to corneal deposits or corneal opacity when topically administered. It should be used with caution in patients presenting with compromised cornea and in instances where the patient is receiving polypharmacy with other phosphate containing eye medications *(see section*

Topical corticosteroids should not be used for longer than one week except under ophthalmic supervision, as prolonged application to the eye of preparations containing corticosteroids has caused increased intraocular pressure. The dose of anti-glaucoma medication may need to be adjusted in these patients. Prolonged use may also increase the hazard of secondary ocular infections.

Cushing's syndrome and/or adrenal suppression associated with systemic absorption of ocular dexamethasone may occur after intensive or long-term continuous therapy in predisposed patients, including children and patients treated with CYP3A4 inhibitors (including ritonavir and cobicistat). In these cases, treatment should be progressively discontinued.

Contact lenses should not be worn during treatment with corticosteroid eye drops due to increased risk of infection.

Systemic absorption may be reduced by compressing the lacrimal sac at the medial canthus for a minute during and following the instillation of the drops. (This blocks the passage of drops via the naso-lacrimal duct to the wide absorptive area of the nasal and pharyngeal mucosa. It is especially advisable in children.)

Visual disturbance

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.

4.5 Interactions with other medicinal products and other forms of interactions

The risk of increased intraocular pressure associated with prolonged corticosteroid therapy may be more likely to occur with concomitant use of anticholinergics, especially atropine and related compounds, in patients predisposed to acute angle closure.

The risk of corneal deposits or corneal opacity may be more likely to occur in patients presenting with compromised cornea and receiving polypharmacy with other phosphate containing eye medications.

The following drug interactions are possible, but are unlikely to be of clinical significance, following the use of Dexamethasone Sodium Phosphate Eye Drops BP Dexamethasone sodium phosphate 0.1% w/v Eye Drops, solution in the eye:

The therapeutic efficacy of dexamethasone may be reduced by phenytoin, phenobarbitone, ephedrine and rifampicin.

Glucocorticoids may increase the need for salicylates as plasma salicylate clearance is increased.

CYP3A4 inhibitors (including ritonavir and cobicistat): may decrease dexamethasone clearance resulting in increased effects and adrenal suppression/Cushing's syndrome. 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 effects.

4.6 Fertility, Pregnancy and Lactation

Topically applied steroids can be absorbed systemically and have been shown to cause abnormalities of foetal development in pregnant animals. Although the relevance of this finding to human beings has not been established, the use of Dexamethasone Sodium Phosphate Eye Drops BP Dexamethasone sodium phosphate 0.1% w/v Eye Drops, solution during pregnancy should be avoided.

Topically applied dexamethasone is not recommended in breastfeeding mothers, as it is possible that traces of dexamethasone may enter the breast milk.

4.7 Effects on ability to drive and use machines

Instillation of this eye drop may cause transient blurring of vision. Warn patients not to drive or operate hazardous machinery until vision is clear.

4.8 Undesirable Effects

Eye disorders

Administration of Dexamethasone Sodium Phosphate Eye Drops BP Dexamethasone sodium phosphate 0.1% w/v Eye Drops, solution to the eye may rarely cause stinging, burning, redness or watering of the eyes.

Prolonged treatment with corticosteroids in high dosage is, rarely, associated with subcapsular cataract. In diseases which cause thinning of the cornea or sclera, perforations of the globe have been known to occur. In addition, optic nerve damage and visual acuity and field defects may arise following long term use of this product.

Not known: vision, blurred (see also section 4.4)

Endocrine disorders

Cushing's syndrome, adrenal suppression may occur due to the use of ocular dexamethasone (see section 4.4). The frequency of these adverse reactions is not known.

The systemic effects of corticosteroids are possible with excessive use of steroid eye drops.

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.

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:

United Kingdom

Yellow Card Scheme; Website: www.mhra.gov.uk/yellowcard

4.9 Overdose

Overdose is unlikely to occur.

5.Pharmacological Properties

5.1 Pharmacodynamic Properties

Pharmacotherapeutic group: Corticosteroids/ antiinfectives/ mydriatics in combination, ATC code: S01B01

Mechanism of action

Dexamethasone is a highly potent and long-acting glucocorticoid. It has an approximately 7 times greater anti-inflammatory potency than prednisolone, another commonly prescribed corticosteroid.

The actions of corticosteroids are mediated by the binding of the corticosteroid molecules to receptor molecules located within sensitive cells. Corticosteroid receptors are present in human trabecular meshwork cells and in rabbit iris ciliary body tissue.

Corticosteroids will inhibit phospholipase A2 thereby preventing the generation of substances which mediate inflammation, for example, prostaglandins. Corticosteroids also produce a marked, though transient, lymphocytopenia. This depletion is due to redistribution of the cells, the T lymphocytes being affected to a greater degree than the B lymphocytes. Lymphokine production is reduced, as is the sensitivity of macrophages to activation by lymphokines. Corticosteroids also retard epithelial regeneration, diminish post-inflammatory neo-vascularisation and reduce towards normal levels the excessive permeability of inflamed capillaries.

The actions of corticosteroids described above are exhibited by Dexamethasone Sodium Phosphate Eye Drops BP Dexamethasone sodium phosphate 0.1% w/v Eye Drops, solution and they all contribute to its antiinflammatory effect.

5.2 Pharmacokinetics

Absorption

When given topically to the eye, dexamethasone is absorbed into the aqueous humour, cornea, iris, choroid, ciliary body and retina. Systemic absorption occurs but may be significant only at higher dosages or in extended paediatric therapy. Up to 90% of dexamethasone is absorbed when given by mouth; peak plasma levels are reached between 1 and 2 hours after ingestion and show wide individual variations.

Biotransformation

Dexamethasone sodium phosphate is rapidly converted to dexamethasone within the circulation. Up to 77% of dexamethasone is bound to plasma proteins, mainly albumin. This percentage, unlike cortisol, remains practically unchanged with increasing steroid concentrations. The mean plasma half life of dexamethasone is 3.6 ± 0.9h.

Distribution

Tissue distribution studies in animals show a high uptake of dexamethasone by the liver, kidney and adrenal glands; a volume of distribution has been quoted as 0.58 l/kg. In man, over 60% of circulating steroids are excreted in the urine within 24 hours, largely as unconjugated steroid.

Elimination

Dexamethasone also appears to be cleared more rapidly from the circulation of the foetus and neonate than in the mother; plasma dexamethasone levels in the foetus and the mother have been found in the ratio of 0.32:1.

5.3 Pre Clinical Safety Data

The use of corticosteroids, including Dexamethasone Sodium Phosphate Eye Drops BP Dexamethasone sodium phosphate 0.1% w/v Eye Drops, solution and its derivatives, in ophthalmology is well established. Little relevant toxicology has been reported, however, the breadth of clinical experience confirms its suitability as a topical ophthalmic agent.

6. Pharmaceutical Particulars

6.1 List of Excipients

Benzalkonium chloride solution
Sodium Metabisulphite
E.D.T.A.Disodium
Di sodium hydrogen orthophosphate
Sterile aqueous base

6.2 Incompatibilities

Not Applicable

6.3 Shelf Life

36 months

6.4 Special precautions for Storage

Store in a cool, dry place at a temperature not exceeding 30^0C. Protect from Light.

6.5 Nature and contents of Container

10ml HDPE screw- ap bottle.

6.6 Special precautions for disposal

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

7. REGISTRANT

Merit Organics Ltd

Plot No 2104/2/A, G.I.D.C , Sarigam , Bhilad,

Dist- Valsad-396155, G jarat , INDIA

8. MANUFACTURER

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Dist- Valsad-396155, G jarat , INDIA

9. DATE OF REVISION OF THE TEXT

Applicable once the registration is obtained.