Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Dexafree 1mg/ml eye drops, solution in single dose container

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

1 ml solution contains 1 mg of dexamethasone phosphate as dexamethasone sodium phosphate.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Eye drops, solution.
Clear, colourless to slightly brown solution.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

For treatment of non-infectious inflammatory conditions affecting the anterior segment of the eye.

4.2 Posology and method of administration

Dexafree 1 mg/ml, eye drops, solution in single-dose container is for ocular use only.

This product should be used only under close ophthalmic supervision.

Posology
The usual posology is of 1 drop 4 to 6 times daily in the affected eye.
In severe cases, treatment may be started with 1 drop every hour but dosage should be reduced to one drop every 4 hours when favourable response is observed. Gradual tapering off is recommended in order to avoid a relapse.

The duration of treatment will generally vary from a few days to a maximum of 14 days.

Elderly patients
There has been wide experience with the use of dexamethasone eye drops in elderly patients. The dosage recommendations given above reflect the clinical data derived from this experience.

Paediatric population
Efficacy and safety has not been established in the paediatric population.
In children, long-term continuous corticosteroid therapy should be avoided due to possible adrenal suppression (see section 4.4).

Method of administration
Dexafree is a sterile solution that does not contain a preservative. The solution from one individual single dose container is to be used immediately after opening for administration to the affected eye(s). For single-use only: since sterility cannot be maintained after the individual single dose container is opened, any remaining contents must be discarded immediately after administration.

Patients should be instructed:
- to wash their hands carefully prior to instillation,
- to avoid contact between the tip of the dispenser and the eye or eyelids,
- to throw away the single-dose container after use.

Nasolacrimal occlusion by compression of lacrimal ducts may reduce systemic absorption.

4.3 Contraindications

- Eye infections not controlled by anti-infectious treatment, such as:
  - Acute purulent bacterial infections including Pseudomonas and mycobacterial infections,
  - Fungal infections,
  - Epithelial Herpes simplex keratitis (dendritic keratitis), vaccinia, varicella zoster and most other viral infections of the cornea and conjunctiva,
  - Amoebic Keratitis,
- Perforation, ulceration and injury of cornea with uncompleted epithelialisation (see also section 4.4),
- Known glucocorticosteroid-induced ocular hypertension,
- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Topical steroids should never be given for an undiagnosed red eye.

Patients should be monitored at frequent intervals during treatment with dexamethasone eye drops. Prolonged use of corticosteroid treatment may result in ocular hypertension/glaucoma (especially for patients with previous IOP induced by steroids or with pre-existing high IOP or Glaucoma) and also cataract formation, especially in children and the elderly population.

The use of corticosteroids may also result in opportunistic ocular infections due to the suppression of host response or to the delay of their healing. In addition, topical ocular corticosteroids may promote, aggravate or mask signs and symptoms of opportunistic eye infections.

Patients with an eye infection should receive local steroid treatment when the infection has been controlled by an effective anti-infectious treatment. Such patients should be carefully and regularly monitored by an ophthalmologist.

In some particular inflammatory conditions such as episcleritis, NSAIDS are the first line treatment, Dexamethasone should be used only if NSAIDS are contra-indicated.

Patients with a corneal ulcer should generally not receive topical dexamethasone except when inflammation is the main cause of healing delay and when the appropriate aetiological treatment has already been prescribed. Such patients should be carefully and regularly monitored by an ophthalmologist.

Thinning of the cornea and sclera may increase the risk of perforations with the use of topical corticosteroids.

This medicine contains 80 micrograms phosphates in each drop. Corneal calcification requiring corneal graft surgery for visual rehabilitation has been reported for patients treated with ophthalmic preparations containing phosphates such as Dexafree. At the first sign of corneal calcification the drug should be withdrawn and the patient should be switched to a phosphate-free preparation.

Posterior subcapsular cataract might occur at cumulative doses of dexamethasone.

Diabetics are also more prone to develop subcapsular cataracts following topical steroid administration.

The use of topical steroids in allergic conjunctivitis is only recommended for severe forms of allergic conjunctivitis not responding to standard therapy and only for a short period.

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.

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.

Wearing of contact lenses during treatment with corticosteroid eye drops should be avoided.

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed.

In case of concomitant treatment with other eye drops, solution, instillations should be spaced out by 15 minutes. Superficial stromal corneal precipitations of calcium phosphate have been reported under combined use of corticosteroids and topical beta-blockers.

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

Pregnancy
Insufficient data are available on the use of Dexafree 1 mg/ml, eye drops, solution in single-dose container in human pregnancy to assess possible harmful effects. Corticosteroids cross the placenta. Teratogenic effects have been observed in animals (see section 5.3). However, there is no evidence to date that teratogenic effects are induced in humans. After systemic use of corticosteroids, at higher doses, effects on the unborn/neonate (intrauterine growth inhibition, inhibition of the function of the adrenal cortex) have been reported. However, these effects have not been reported for ocular use.
As a precautionary measure, it is preferable to avoid the use of Dexafree 1 mg/ml, eye drops, solution in single-dose container during pregnancy.

Breastfeeding
It is not known whether this medicine is excreted in breast milk. However the total dose of dexamethasone is low, Dexafree 1 mg/ml, eye drops, solution in single-dose container can be used during lactation.

Fertility
There are no data on potential effects of Dexamethasone 1 mg/ml on fertility.

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed.
As with any eye drops, temporarily blurred vision or other visual disturbances may affect the ability to drive or use machines. If blurred vision occurs, the patient must wait until the vision is clear before driving or using machines.

4.8 Undesirable effects

Endocrine disorders:
- Not known (cannot be estimated from the available data): Cushing's syndrome, adrenal suppression* (see section 4.4)

Eye disorders:
- Very common (≥1/10): Increase of the intra-ocular pressure*.

- Common (≥1/100 to <1/10): Discomfort*, irritation*, burning*, stinging*, itching* and blurred vision (see also section 4.4)*.
- Uncommon (≥1/1,000 to <1/100): Allergic and hypersensitivity reactions, delayed wound healing, posterior capsular cataract*, opportunistic infections, glaucoma*.
- Very rare (≥1/10,000, including isolated reports): Conjunctivitis, mydriasis, facial oedema, ptosis, corticosteroid-induced uveitis, corneal calcifications, crystalline keratopathy, changes in corneal thickness*, corneal oedema, corneal ulceration and corneal perforation.

** see section Description of selected adverse reactions*

Description of selected adverse reactions
Increase of the intra-ocular pressure, glaucoma and cataract may occur. Prolonged use of corticosteroid treatment may result in ocular hypertension/glaucoma (especially for patients with previous IOP induced by steroids or with pre-existing high IOP or Glaucoma) and also cataract formation, Children and elderly patients may be particularly susceptible to steroid-induced IOP rise (see section, 4.4).
Increase of the intra-ocular pressure induced by corticosteroid topical treatment has been generally observed within 2 weeks of treatment (see section 4.4.).
Diabetics are also more prone to develop subcapsular cataracts following topical steroid administration.
Discomfort, irritation, burning, stinging, itching and blurred vision frequently may occur immediately after instillation. These events are usually mild and transient and have no consequences.
In diseases causing thinning of the cornea, topical use of steroids could lead to perforation in some cases (see section 4.4).
Depression of adrenal function associated with systemic absorption of the product may occur when the instillations are administered with a frequent dosing schedule (see also sections 4.2 and 4.4).

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 HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; e-mail: medsafety@hpra.ie

4.9 Overdose

In the case of topical overdosage, the treatment should be stopped. In case of prolonged irritation, the eye(s) should be rinsed with sterile water.
The symptomatology due to accidental ingestion is not known. As with other corticosteroids however, the physician may consider gastric lavage or emesis.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: OPHTHALMOLOGICALS, ANTIINFLAMMATORY AGENTS, Corticosteroids, plain, ATC code: S01B A01
Dexamethasone sodium phosphate is a hydrosoluble inorganic ester of dexamethasone. It is a synthetic corticosteroid with an anti-inflammatory and anti-allergic action. Dexamethasone has more potent anti-inflammatory action compared to hydrocortisone (approximately 25:1) and prednisolone (approximately 5:1).

5.2 Pharmacokinetic properties

Due to its hydrophilic properties, dexamethasone sodium phosphate is barely absorbed by the intact epithelium of the cornea.
Following absorption via the eye and the nasal mucosa, dexamethasone sodium phosphate is hydrolyzed in the system

to dexamethasone.
Afterwards, dexamethasone and its metabolites are mainly eliminated via the kidneys.

5.3 Preclinical safety data

Mutagenic and tumorigenic potential
Present findings yield no indications of clinically relevant genotoxic properties of glucocorticoids.

Reproductive toxicity
In animal experiments, corticosteroids have been shown to produce foetal resorptions and cleft palate. In the rabbit corticosteroids have produced foetal resorptions and multiple abnormalities involving the head, ears, limbs and palate. In addition, intrauterine growth inhibition and changes of functional development of the central nervous system have been reported.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Disodium edetate
Disodium phosphate dodecahydrate
Sodium chloride
Water for injections

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

After first opening of the sachet:
For sachet of 5 or 10 single-dose containers: use the single-dose containers within 15 days.

After opening of the single-dose container - use immediately and discard the single-dose container after use.

6.4 Special precautions for storage

Keep the single-dose containers in the sachet, in order to protect from light.

6.5 Nature and contents of container

0.4 ml in single-dose low density polyethylene container packed in sachets; box of 10, 20, 30, 50 or of 100 single-dose containers.
Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.

7 MARKETING AUTHORISATION HOLDER

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8 MARKETING AUTHORISATION NUMBER

PA1107/005/001

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10 DATE OF REVISION OF THE TEXT

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