Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Dexeta 1.37 mg/ml eye drops, solution in single dose container

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 1 ml of solution contains 1.37 mg dexamethasone phosphate equivalent to 1.5 mg dexamethasone sodium phosphate.
Each single-dose container of 0.3 ml contains 8.3 drops of 36 microlitres.
Each drop contains 54 micrograms dexamethasone sodium phosphate.

Excipients with known effect:
1 ml of solution contains 1.465 mg monobasic sodium phosphate monohydrate and 10 mg disodium phosphate dodecahydrate.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Eye drops, solution

Clear and colourless solution, practically free from particles.
pH: 6.7 – 7.7
Osmolality: 0.270 – 0.320 Osmol/kg

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Dexeta is indicated for the treatment of steroid responsive, non-infectious, inflammatory conditions of the anterior segment of the eye.

4.2 Posology and method of administration

Posology

The dose is one drop of Dexeta into the conjunctival sac three to four times daily. The dose may be adjusted according to clinical requirements.

Paediatric population

The safety and efficacy have not been established in the paediatric population. No data are available.

Long-term continuous corticosteroid therapy should be avoided due to possible adrenal suppression (see section 4.4).

Method of administration
For ocular use only. The solution from one individual single dose container is to be used to the affected eye(s) immediately after opening for administration.
Patients should be informed of the correct handling of the single-dose container.

Instructions for use
Patients should be informed of the correct handling of the single-dose container.

1. Wash hands thoroughly before putting in the eye drops.
2. Make sure the single-dose container is intact.
3. Detach the single-dose container from the strip.

4. Open by turning the flap of the unit without pulling.

5. Sit or lie down and tilt head back and look up. Using your thumb and forefinger, gently and carefully pull the lower eyelid down.
6. Do not allow the tip of the single-dose container to touch the eye or eyelids, or any other surface, so to avoid possible contamination.

Since sterility cannot be maintained after the individual single dose container is opened, any remaining contents must be discarded after administration.
Nasolacrimal occlusion by compression of lacrimal ducts may reduce systemic absorption (see Section 4.4).

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

Dexeta is contraindicated in patients with:

- intraocular hypertension
- herpes simplex
- viral infections of the cornea at ulcerous stage
- conjunctivitis with ulcerative keratitis, early stage (Fluorescein test +)
- tuberculosis and mycosis of the eye
- acute purulent ophthalmias
- purulent conjunctivitis
- purulent herpetic blepharitis
- hordoleum
- corneal lesions and abrasions

4.4 Special warnings and precautions for use

Prolonged use of corticosteroids may result in an increase of intraocular pressure, therefore it is recommended to monitor the intraocular pressure if corticosteroids are used for two weeks or longer. This is especially important in paediatric patients because the risk of corticosteroid-induced, ocular hypertension may be greater in children and may occur earlier than in adults. Long-term use (1 – 4 years) of ophthalmic corticosteroids, especially at highdoses, as well as individual sensitivity, have been known to cause crystalline opacification (posterior capsular opacification).

Particular attention should be given to disorders associated to corneal thinning.
Local administration of corticosteroids to patients with bacterial, viral or fungal conjunctivitis may mask signs of the progression of infection.

In viral infections, the use of steroids may worsen/exacerbate the condition, which may lead to irreversible corneal opacification (see section 4.3).

The product is not recommended for the treatment of herpetic keratitis but it may be used if required under close supervision of a doctor. Use of steroids may delay wound healing of damaged tissue and increase the incidence and spread of 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 (see section 4.5).

Dexeta is not recommended during pregnancy and lactation.

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).

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.

This medicine contains 0.13 mg phosphates in each drop which is equivalent to 3.66 mg/ml (see section 4.5).

Paediatric population
In children the product should be administered only after a careful benefit-risk assessment and under strict medical control.

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed.

If the use of multiple ophthalmic products is required, patients must be informed that instillations should be spaced out by 5 minutes and to use the ointments last.

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 (see section 4.4).

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 (see section 4.4).

The following drug interactions are possible, but are unlikely to be of clinical significance, following the use of Dexamethasone sodium phosphate 1.5 mg/ml in the eye:

- The therapeutic efficacy of dexamethasone may be reduced by phenytoin, phenobarbital and other sedative hypnotics, ephedrine and rifampicin.
- Dexamethasone can decrease the therapeutic effect of anticholinesterases and antiviral medication.
- 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

Pregnancy
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 1.5 mg/ml eye drops, solution during pregnancy should be avoided.

Breast-feeding

It is not known whether this medicine is excreted in breast milk.
The use of Dexeta eye drops, solution is not recommended during breast-feeding.

Fertility
There are no data on potential effects of Dexamethasone sodium phosphate 1.5 mg/ml eye drops on fertility.

4.7 Effects on ability to drive and use machines

Instillation of Dexeta may cause transient blurring of vision. Patients should be advised not to drive or operate machinery until vision is clear.

4.8 Undesirable effects

Possible undesirable effects due to corticosteroids are the following:

Endocrine disorders
Frequency not known**:**
- Cushing's syndrome, adrenal suppression* (see section 4.4).

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

Common (≥1/100 to <1/10):
- eye pruritus;
- abnormal sensation in the eye*.

Uncommon (≥1/1,000 to <1/100):
- subcapsular cataract formation*;
- delayed wound healing.

Very rare (<1/10,000, including isolated reports)
- open globe injury*;
- corneal calcification*.

Infections and infestations
Uncommon (≥1/1,000 to <1/100):
- worsening/exacerbation of *Herpes simplex* or fungal infections;

In all the above cases, patients should discontinue using the eye drops and start an adequate treatment.

* See 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 the national reporting system:
HPRA Pharmacovigilance
Website: www.hpra.ie

4.9 Overdose

Cases of overdose have never been reported.
In the case of topical overdosage, rinse thoroughly.
In case of prolonged irritation or undesired eye contact, the eye(s) should be rinsed with warm 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: Anti-inflammatory agents, Corticosteroids, plain, ATC code: S01BA01

Mechanism of action
Dexamethasone sodium phosphate is a corticosteroid with a high anti-inflammatory activity, 25 times greater than hydrocortisone. Like all corticosteroids it mainly acts by inhibiting the release of arachidonic acid which is the forerunner of the most important mediators of inflammation: prostaglandins and leukotriens. Dexamethasone induces the synthesis of a protein, lipomodulin, which in turn inhibits the action of the enzyme responsible for the release of arachidonic acid: phospholipase A2. Corticosteroids are believed to act by the induction of vascular endothelial adhesion molecules, cyclooxygenase 1 or 2 (COX- 1 or 2), and cytokine expression. This results in decreased expression of proinflammatory mediators and suppression of circulating leukocytes that adhere to the vascular endothelium, and their migration into inflamed ocular tissues.
Dexamethasone is a corticosteroid with a markedly potentiated anti-inflammatory activity and minimal mineralocorticoid activity with respect to other steroids, thus one of the most potent anti- inflammatory agents available.

5.2 Pharmacokinetic properties

Corticosteroids usually reach intraocular therapeutic concentrations after instillation into the conjunctival sac. However, the degree of penetration depends upon molecular characteristics and chemical form.

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.

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. Up to 77% of dexamethasone is bound to plasma proteins, mainly albumin. This percentage, unlike cortisol, remains practically unchanged with increasing steroid concentrations.

Biotransformation

Dexamethasone sodium phosphate is rapidly converted to dexamethasone within the circulation (as well as in the tear).

Elimination

The mean plasma half life of dexamethasone is 3.6 ± 0.9h. 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 Preclinical safety data

Dexamethasone demonstrated to be well tolerated in laboratory animals (rabbits and rats) after local application for up to six months.
The toxicity symptoms of dexamethasone found in various animal species after oral administration are related to the adrenocorticosteroid effects and include the alteration of the adreno-pituitary axis and slight anaemia.
Signs of toxicity were found in the stomach, liver, adrenal and pituitary glands, lungs and spleen of laboratory animals.
In the studies carried out following local administration, most of these conditions were absent or rare.

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

Sodium citrate
Sodium phosphate monobasic monohydrate
Disodium phosphate dodecahydrate
Purified water

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years

The single-dose containers must be used immediately after opening; any remaining contents must be discarded.

After aluminium sachet first opening, the single-dose containers remaining in the sachet have to be used within 28 days; after this period the unused single-dose containers must be discarded.

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

Dexeta 1.37 mg/ml eye drops, solution in single dose container is contained in low density polyethylene (LDPE) single-dose containers with 0.3 ml of eye drops. The single-dose containers are moulded in 5 sealed units strip, which in turn are wrapped in an aluminium sachet and packaged inside a carton box.
The carton box contains 2 or 4 aluminium sachets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

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

7 MARKETING AUTHORISATION HOLDER

SIFI S.p.A.
Via Ercole Patti 36
Aci Sant'antonio
CT
95025
Italy

8 MARKETING AUTHORISATION NUMBER

PA23335/001/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 27th November 2020
Date of renewal 21st August 2024

10 DATE OF REVISION OF THE TEXT

March 2024