SUMMARY OF PRODUCT CHARACTERISTICS

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1. NAME OF THE MEDICINAL PRODUCT

Ronic 1 mg/ml eye drops, solution.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Dexamethasone phosphate 1 mg/ml (equivalent to 1.093 mg/ml dexamethasone sodium phosphate)

Excipient(s) with known effect:

Benzalkonium chloride (solution at 10%) – 0.001 ml/ml
Phosphate buffers (monosodium phosphate and disodium phosphate) – 5.6 mg/ml

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Eye drops, solution
Clear, colourless and odourless solution.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Ronic 1 mg/ml eye drops, solution is indicated in the treatment of conjunctival disorder (conjunctivitis, corneal-conjunctival burning, blepharoconjunctivitis), iridocyclitis, toxoplasmosis chorioretinal foci and severe allergic conjunctival conditions.
Ronic is primarily indicated in inflammatory conditions and should not be used in acute eye infections.
While using this medicine a close medical supervision should be performed.

4.2 Posology and method of administration

The posology and duration of treatment should be instituted by the doctor, case by case.

Overall the posology is the following:
- Severe acute disorders: 1 drop every hour;
- Less severe acute disorders: two drops 3 to 6 times a day.

Treatment should not be interrupted abruptly.

4.3 Contraindications

- Hypersensitivity to the active substance (dexamethasone sodium phosphate) or to any of the excipients listed in section 6.1.
- In case of herpetic or mycotic keratitis, ocular tuberculosis, varicella and infection caused by vaccinia virus. It is also contraindicated in patients with history of glaucoma and immunosuppressed patients.

4.4 Special warnings and precautions for use

Dexamethasone may delay the healing of keratic lesions and should be used with caution in these cases.

Ronic should be used with caution in patients with ocular hypertension or previous history of intraocular pressure increase when using topical corticosteroids.

Contact lens users:
Ronic contains 0.1 benzalkonium chloride in each ml of solution.
Benzalkonium chloride may be absorbed by soft contact lenses and may change the colour of the contact lenses. Remove contact lenses before using this medicine and put them back 15 minutes afterwards. Benzalkonium chloride has been reported to cause eye irritation, symptoms of dry eyes and may affect the tear film and corneal surface. Should be used with caution in dry eye patients and in patients where the cornea may be compromised. Patients should be monitored in case of prolonged use.

Ronic contains phosphate buffers. This medicinal product contains 5.6 mg of phosphates in each ml of solution. See section 4.8.

Like in all preparations containing corticosteroids and topically used in ophthalmology, one should consider the systemic absorption and not use this medicine beyond the duration indicated by the doctor, who should monitor the patients' intraocular pressure.

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 persistent 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.

Paediatric population
It should be used with caution in children up to 2 years old, since it may increase the risk of renal suppression. In such case, it should not be used beyond 5 days.

After first opening the bottle, use within 28 days.

4.5 Interaction with other medicinal products and other forms of interaction

- Antiglaucoma agents - chronic or intensive use of ophthalmic corticoids may increase the intraocular pressure and reduce the efficacy of the antiglaucoma agents.

- Anticholinergics, particularly atropine and related compounds - the risk of intraocular hypertension may increase with the extended use of ophthalmic corticosteroids; such increase may occur with higher probability during the simultaneous use of cycloplegic/mydriatic agents in patients with acute angle-closure glaucoma predisposition.

- 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.

Systemic absorption is minimal and interactions are not expected.
However, it should be considered that the effects of hypoglycaemic agents (including insulin), antihypertensives and diuretic agent are antagonized by glucocorticoids.

4.6 Fertility, pregnancy and lactation

Although the studies performed with ophthalmic corticoids do not show malformation effects on gestation or other problems during lactation, the doctor should balance the benefit/risk ratio.

4.7 Effects on ability to drive and use machines

After instillation of the drops, the vision may be temporarily blurred, so caution is advised when driving or using machines.

4.8 Undesirable effects

Common (≥1/100, <1/10): discomfort; burning; stinging sensation; (temporary) blurred vision;
These effects are normally mild and temporary.

Uncommon (≥1/1000, <1/100): conjunctival congestion; dryness around the eyes; ocular irritation; tearing; glaucoma; increase of intraocular pressure; cataract formation particularly in diabetics; increased risk of hyperglycaemia in diabetic patients; risk of opportunistic infections development; risk of keratic calcification.

Very rare (<1/10000): 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.

Not known (cannot be estimated from the available data): cushing's syndrome, adrenal suppression, persistent blurred vision (see 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

No cases of overdose are described.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Ophthalmologicals. Antiinfmmatory agents. Corticosteroids, plain.
ATC code: S01BA01

Glucocorticoids (such as dexamethasone) get diffused through the citoplasmatic membrane and set on a specific intracytoplasmic protein, establishing a receptor complex. Inside the cell, that complex shall settle on the nuclear chromatin; that receptor spot is specific and the complex is activated and participates in the synthesis of the mRNA. Thus, the ribosomes cause glucocorticoid effects at a cellular level, either direct effects (on the cell itself), or indirect ones (on other cells or tissues).
The specific protein stops the development of arachidonic acid preventing its cascade from being created, which is the source of the development of tissues responsible for inflammation.

5.2 Pharmacokinetic properties

Dexamethasone sodium phosphate is a hydrophilic compound which undergoes hydrolysis by the enzymes on the tear film and on the cornea becoming a lipophilic compound that easily penetrates the corneal intact epithelium.

5.3 Preclinical safety data

Dexamethasone is a substance that, from a toxicological point of view, may be used on humans and does not show any issue that requires special measures or that prevent it from being used as a therapeutic agent.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Monosodium phosphate
Disodium phosphate
Benzalkonium chloride 10% solution
Sodium thiosulfate
Sodium chloride
Sodium edetate
Highly purified water
Hydrochloric acid (for pH adjustment)
Sodium hydroxide (for pH adjustment)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.
After first opening, use within 28 days.

6.4 Special precautions for storage

Do not store above 25ºC.

6.5 Nature and contents of container

Ronic eye drops, solution is supplied in opaque white LDPE bottles with transparent LDPE dropper insert and opaque white HDPE cap with tamper-proof closure, containing 5 ml of the solution.

6.6 Special precautions for disposal and other handling

Open the container cap and exert a slight pressure on it, releasing the liquid drop by drop at the recommended dose.

7. MARKETING AUTHORISATION HOLDER

Laboratório Edol - Produtos Farmacêuticos, S.A.
Av. 25 de Abril, 6-6A
2795-225 Linda-a-Velha
Portugal

8. MARKETING AUTHORISATION NUMBER(S)

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

10. DATE OF REVISION OF THE TEXT

04/2018