SUMMARY OF PRODUCT CHARACTERISTICS

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1. NAME OF THE MEDICINAL PRODUCT

DEXACOLLYRE eye drops solution 0.1 % w/v

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml of solution contains 1 mg of dexamethasone.
Excipients with known action: Each mL of solution contains 0.1 mg benzalkonium chloride (see section 4.4).

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Eye drops, solution

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Allergic conditions of conjunctiva, cornea and eyelids, regardless of allergenic cause, symptomatic. Aseptic inflammatory conditions of the uvea, sclera and epidural, as well as the cornea. They are also administered postoperatively in intra-bulb surgeries, bulb injuries and keratoplasties. They can be administered to adenovirus infections and common bacteria (conjunctivitis) in the early intense phases of inflammation but under full chemotherapy coverage. In general, however, it is advisable to be avoided for all infectious conditions of the eye.

4.2 Posology and method of administration

The dose is one to two drops 3-5 times a day in the conjunctival sac. In severe cases, the instillation can be done per hour. The duration of treatment varies depending on the type of lesion and the therapeutic response.

Paediatric patients
The safety and efficacy of DEXACOLLYRE in children under 18 years of age have not been established.

Elderly population
No differences in safety or efficacy have been observed between older and younger patients.

Use in patients with hepatic and renal impairment
The safety and efficacy of DEXACOLLYRE in patients with hepatic or renal impairment have not been established.

Method of administration

For ocular use only.

Patients should be instructed to shake the bottle well before use.

After removing the cap, and if the safety collar is loose, it should be removed before using the medicine.

To prevent contamination of the dropper nozzle and solution, care must be taken not to touch the eyelids, surrounding areas or other surfaces with the dropper tip of the bottle.

Gentle eyelid closure and nasolacrimal occlusion are recommended after administration. This can reduce the systemic absorption of the drug administrated through the ocular route and lead to a reduction in systemic side effects.

If more than one topical ophthalmic product is used, there should be a five-minute interval between successive administrations. Eye ointments should be administered last.

4.3 Contraindications

- Hypersensitivity to dexamethasone or to any of the excipients listed in section 6.1.
- Acute, untreated bacterial infections
- Herpes simplex virus keratitis (dendritic keratitis)
- Smallpox, chickenpox and other viral infections of the cornea or conjunctiva.
- Fungal diseases of the ocular structures or untreated parasitic infections of the eyes.
- Mycobacterial ocular infections, such as ocular tuberculosis.
- Individual or hereditary history of glaucoma.

4.4 Special warnings and precautions for use

Corticosteroids should not be administered without prior slit lamp biomicroscopy to rule out corneal damage from herpes simplex virus.
Chronic administration should be avoided as much as possible.
Prolonged use of topical ocular corticosteroids can lead to ocular hypertension and / or glaucoma, optic nerve damage, decreased visual acuity and visual field deficits, and posterior subcapsular cataract formation.

In patients receiving prolonged ocular treatment with corticosteroids, the intraocular pressure should be monitored regularly and frequently.

This is especially important in pediatric patients, as the risk of ocular hypertension due to corticosteroids may be higher in children and occur earlier than in adults. DEXACOLLYRE is not approved for use in pediatric patients.

The risk of increased intraocular pressure and/or cataract formation due to corticosteroids is increased in predisposed patients (e.g. diabetes).

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

In case of using this medicine for more than 10 days, it is recommended to check the intraocular pressure and the lens frequently. Of the ocular corticosteroids, dexamethasone (0.1%) and prednisolone (1%) cause the largest increase in intraocular pressure.

Corticosteroids can reduce resistance and contribute to bacterial, viral, fungal or parasitic infections and cover the clinical signs of an infection.

Fungal infection should be considered in patients with persistent corneal ulcers. If a fungal infection occurs, treatment with corticosteroids should be discontinued.

Topical ocular corticosteroids may slow the healing of corneal wounds. Topical NSAIDs are also known to slow or delay healing. Concomitant use of topical NSAIDs and topical steroids may increase the likelihood of healing problems (see section 4.5).

In diseases that cause thinning of the cornea or the sclera, perforations have been observed after the use of topical corticosteroids.
Avoid using contact lenses during the treatment of an ocular inflammation.
DEXACOLLYRE contains benzalkonium chloride which can cause eye irritation and is known to discolor soft contact lenses. Contact with soft contact lenses should be avoided. In case patients are allowed to wear contact lenses, you should advise them to remove their contact lenses before applying DEXACOLLYRE and wait at least 15 minutes before putting them on again.

Athletes should be careful because this medicine contains an active ingredient that can give a positive result on a possible anti-doping control.

Visual disturbance

Visual disturbance with systemic and topical corticosteroid use may be reported. If a patient is experiencing symptoms such as blurred vision or other visual disturbances, then the patient should be referred to an ophthalmologist for the evaluation of possible causes that may include cataract, glaucoma or rare diseases such as central serous choroidal dementia and have been reported after the use of systemic and topical corticosteroids.

In case of hypersensitivity, stop the treatment.

4.5 Interactions with other medicinal products and other forms of interaction

Concomitant use of topical steroids and topical NSAIDs may increase the likelihood of corneal healing problems.

No interaction studies have been performed.

CYP3A4 inhibitors (including ritonavir and cobicistat) may reduce dexamethasone clearance resulting in increased effects and suppression of adrenal / Cushing's syndrome. The combination should be avoided unless the benefit outweighs the increased risk of systemic side effects of corticosteroids, where patients should be monitored for systemic effects of corticosteroids.

4.6 Fertility, pregnancy and lactation

Fertility
No studies have been performed to evaluate the effect of topical ocular administration of dexamethasone on fertility. There are limited clinical data to evaluate the effect of dexamethasone on male and female fertility. Dexamethasone showed no adverse effects on fertility in a rat model prepared with chorionic gonadotropin.

Pregnancy
There are no adequate or well-controlled studies evaluating DEXACOLLYRE in pregnant women. Prolonged or repeated use of corticosteroids during pregnancy has been associated with an increased risk of intrauterine growth retardation. Babies born to mothers who have received significant doses of corticosteroids during pregnancy should be closely monitored for signs of hypoadrenalism (see section 4.4).

Studies in z experimental animals have shown reproductive toxicity after systemic administration. Ophthalmic administration of 0.1% dexamethasone also led to fetal abnormalities in rabbits (see section 5.3).

Dexamethasone has been shown to be teratogenic in topically administered ocularly to mice and rabbits at multiple therapeutic doses.

DEXACOLLYRE is not recommended during pregnancy or in women of childbearing potential without the use of contraception.

Lactation
It is not known whether DEXACOLLYRE is excreted in human milk. No data are available on the excretion of dexamethasone in human milk. It is unlikely that the amount of dexamethasone is detectable in human milk or capable of causing clinical effects in the infant after topical ocular administration. The risk to breast-fed infants cannot be ruled out.

To reduce systemic absorption, see section 4.2.
It must be decided whether to discontinue breast-feeding or to discontinue / avoid treatment with DEXACOLLYRE, taking into account the benefit of breast-feeding for the child and the benefit of treatment for the woman.

4.7 Effects on ability to drive and use machines

Transient blurred vision or other visual disturbances may affect the ability to drive or use machines. If blurred vision occurs after instillation, the patient should wait until his or her vision is clear before driving or operating machinery.
DEXACOLLYRE has no or negligible effect on the ability to drive and use machines.

4.8 Undesirable effects

Summary of the safety profile
In clinical trials, the most common adverse reaction was ocular discomfort.

Summary of side effects in a table

The following side effects listed in the table below have been observed in clinical trials or post-marketing experience with DEXACOLLYRE, and are classified according to the

following rule: very common (≥ 1/10), common (≥ 1/100) to <1/10), uncommon (≥ 1 / 1,000 to <1/100), rare (≥ 1 / 10,000 to <1 / 1,000), very rare (<1 / 10,000) or unknown (cannot be estimated based on available data). Within each frequency category, adverse reactions are presented in descending order of severity.

System Organ Classification	Frequency	Adverse reaction
Nervous system disorders	Uncommon	dysgeusia
	Not known	dizziness, headache
Immune system disorders	Not known	hypersensitivity
Eye disorders	Common	ocular discomfort
	Uncommon	keratitis, conjunctivitis, dry eye, dry corneal conjunctivitis, corneal staining, photophobia, blurred vision, itching of the eye, foreign body sensation in the eyes, increased tearing of the eye, abnormal sensation of the eye, eyelid margin crusting, eye irritation (flaring, stinging), hyperemia of the eye.
	Not known	blurred vision (see also section 4.4)
	Rare	hyperemia of the conjunctiva, confluent bubbles after cataract surgery.
	Not known	glaucoma, ulcerative keratitis, increased intraocular pressure, decreased visual acuity, corneal erosion, eyelid drooping, eye pain, mydriasis.
Disorders of the endocrine system	Not known	Cushing's syndrome, adrenal suppression, adrenal insufficiency

Description of selected adverse reactions

Prolonged use of topical ophthalmic corticosteroids may result in increased intraocular pressure with damage to the optic nerve, reduced visual acuity and visual field defects, and to posterior subcapsular cataract formation (see section 4.4).

Due to the corticosteroid component, in diseases causing thinning of the cornea or sclera there is a higher risk for perforation especially after long treatments (see section 4.4).

Corticosteroids may reduce resistance and aid in the establishment of infections (see section 4.4).

Rarely, systemic side effects from absorption to chronic administration have been reported.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorization 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.

4.9 Overdose

An ocular overdose of DEXACOLLYRE can be flushed out of the eye (s) with lukewarm water.

Due to the characteristics of this formulation, no toxic effects are expected with an ocular overdose of this product, or in case of accidental ingestion of the contents of a bottle.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic Group: Ophthalmologicals, Anti-inflammatory Agents corticosteroids
ATC Code: S01BA01

Action mechanism
DEXACOLLYRE contains 1 mg dexamethasone per mL eye drops.

The exact mechanism of the anti-inflammatory action of dexamethasone is unknown. Inhibits many inflammatory cytokines and exhibits multiple glucocorticoids and saline effects. Dexamethasone inhibits the inflammatory response to irritant agents of mechanical, chemical or immune nature edema, inhibits neovascularization, fibroblast proliferation and other productive phenomena that accompany the final stages of the inflammatory process. Inhibits phagocytosis and lymphatic tissue response.

Pharmacodynamic effects
Dexamethasone is one of the most potent corticosteroids, having a greater anti-inflammatory effect than prednisolone or hydrocortisone.

Clinical efficacy and safety
The safety and efficacy of dexamethasone have been established in adult clinical trials, in the published literature, and in post-marketing experience of the product.

Paediatric population
The safety and efficacy of dexamethasone have not been studied in children. However, dexamethasone has been reported to be safe for pediatric use in general.

5.2 Pharmacokinetic properties

Absorption
Following topical ocular administration, dexamethasone is detectable after 30 minutes in the aqueous humor and reaches a maximum of 90 to 120 minutes at an average concentration of 31ng /mL. Low but detectable concentrations are observed in the aqueous humor after 12 hours. The oral bioavailability of dexamethasone ranged from 70-80% in normal individuals and patients.

Allocation
Following intravenous administration, the steady-state volume of distribution was 0.58 L/kg. *In vitro*, no change in plasma protein binding was observed in humans with dexamethasone concentrations ranging from 0.04 to 4 μg/mL, with an average plasma protein binding of 77.4%.

Biotransformation
Following oral administration, two major metabolites were recovered. 60% of the dose was recovered as 6β-hydroxydexamethasone and up to 10% was recovered as 6β-hydroxy-20-dihydrodexamethasone.

Elimination
Following intravenous administration, systemic clearance was 0.125 L/hr/kg. Following oral administration, 2.6% of the unchanged starting drug was recovered in the urine while 70% of the dose was recovered as metabolites. Following systemic administration, the half-life has been reported to be 3-4 hours, but has been found to be slightly longer in men. This observed difference was not attributed to changes in systemic clearance but to differences in distribution volume and body weight.

Linear/non-linear pharmacokinetics
Non-linear pharmacokinetics was observed after oral administration at doses between 0.5 and 1.5 mg where the area under the curve was less proportional to the oral dose.

Pharmacokinetic/pharmacodynamic relationship (s)
No pharmacokinetic/pharmacodynamic relationship was determined after topical ocular administration.

Pharmacokinetics of Special Populations
The pharmacokinetics of systemic dexamethasone did not differ significantly in patients with renal impairment compared with normal subjects. Pharmacokinetics in the pediatric population varied between age groups but no significant differences were observed between patients.

5.3 Preclinical safety data

Non-clinical data do not reveal a particular risk to humans at the recommended clinical dose, based on conventional studies of repeated dose toxicity, genotoxicity, carcinogenicity or toxicity in reproduction and development.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium Chloride, Sodium Phosphate Monobasic Monohydrate, Sodium Phosphate Dibasic Dihydrate, Edetate Disodium, Sodium Metabisulfite, Benzalkonium Chloride, Water for Injections.

6.2 Incompatibilities

Due to the presence of quaternary ammonium salts, these eye drops are not compatible with fluorescein sodium, pilocarpine nitrate, sulfacetamide sodium, silver salts, boric acid and salicylate. For information on using this product with contact lenses see Section 4.4.

6.3 Shelf life

24 months
Discard 4 weeks after first opening the bottle.

6.4 Special precautions for storage

Do not store above 30ºC.

6.5 Nature and contents of container

Available in a 5 mL plastic vial with white dropper and white cap.

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

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8 MARKETING AUTHORISATION NUMBER(S)

35759/16

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

19-10-1992/6-2-2007

10 DATE OF REVISION OF THE TEXT

17/9/2020