1. Name of the medicinal Product

Dexamethasone Sodium Phosphate & Gentamicin Sulfate Eye/Ear Drops – DEEXA-G

2. Qualitative and Quantitative Composition

Qualitative declaration

Dexamethasone Sodium Phosphate USP

Gentamicin Sulfate BP

Excipient(s) with known effect: Benzalkonium Chloride 0.0001 ml

Quantitative declaration

For full list of Excipients, see section 6.1.

3. Pharmaceutical Form

Eye Drops & Ear Drops

Distribution category POM

A clear colourless to pale yellow colour clear solution

4. Clinical Particulars

1. Therapeutic Indications

Dexamethasone and Gentamicin eye/ ear drops It is used to treat infections of the anterior eye including conjunctivitis, keratitis, blepharitis, and hordeolum, inflammation in otitis externa with eczema present; short term treatment and caused by gentamicin-sensitive pathogens; allergic inflammation of the anterior eye with bacterial superinfection. The safety and efficacy of this product has not been established in children below 2 years of age

2. Posology and Method of Administration

Posology

Instill 1 drop 4-6 times daily into the conjunctival sac.

Method of administration: ocular use and auricular use.

Eye: Dexamethasone and gentamicin eye/ ear drops instill, one or two drops every 2-3 hours should be applied topically to the eye up to six times a day. Note: In severe conditions the treatment may be initiated with one drop every 2 hours, the dosage should then be gradually reduced as the inflammation subsides fifteen to twenty minutes initially. Treatment of topically eye drops should normally not exceed a period of 2 weeks, or at most 3 weeks.

The exact duration of combine component of products for eye therapy should be based on the physician‘s decision when all factors including efficacy, severity of the symptoms, and potential side effects are considered. Eye drops should be applied in such a way that any contact of the dropping insert with the eye or skin is avoided.

Ear: Dexamethasone and gentamicin eye/ ear drops instill in ear, one drops are usually given in to affected ear three or four times day and at night or more frequently if required As per physician direction on how often to give the drops to patients.

Paediatric population: No data available

Directions for Use: Shake the bottle well before use and “After cap is removed, if tamper evident snap collar is loose, remove before using product” Do not touch dropper tip or other dispensing tip to any surface since this may contaminate solutions. Discard any unused medicine after the completion of the course of therapy or within 4 weeks after opening the bottle.

3. Contraindications

Hypersensitivity to any corticosteroids and aminoglycoside antibiotic group. Should not be

administered to patients with a known allergy to gentamicin and other aminoglycosides.

Evidence exists that gentamicin may cause neuromuscular blockade and is therefore contra-

indicated in myasthenia gravis and related conditions. Perforated tympanic membrane.

herpes corneae superficialis, injuries and ulcerations of the cornea, closed and open-angle

glaucoma, tuberculous or fungal infections of the eye, solely bacterial infections.

4. Special warnings and precautions for use

For external use only not for injection.

Dosage and usage often depends on the severity of the condition, as well as the patient’s medical history and current health condition. If irritation persists or increases, discontinue the use and consult physician.

Before taking, inform to physician if you are diagnosed with any fungal infections, viral infections such as herpes simplex or varicella, or parasitic infections such as amoebiasis. Do not use if you have tuberculosis, damaged cornea, ulceration, open lesions with incomplete formation of the covering tissue and increased pressure inside the eye. vision problems, severe pain in the eye, glaucoma (raised pressure in the eye), eye injury, or have undergone eye surgery or using any other eye drops or eye ointment. Inform your doctor immediately if you notice swelling or weight gain around the trunk or in the face, as it may be a sign of Cushing’s syndrome (high levels of cortisol in the body). Do not use for longer than recommended by your doctor as it may suppress adrenal gland function and may increase the risk of cataracts (clouding of the eye) and also increases the risk of a second infection.

Pregnancy and Lactation: It should only be used when considered essential by physician and only if the anticipated benefit outweighs the potential risk.

Excipients with known effect: It contain 0.0001 ml Benzalkonium chloride may 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. Contact lenses should not be worn during treatment with dexamethasone and gentamicin eye/ ear drops.
This formulation contains Benzalkonium chloride as a preservative which may be deposited in soft contact lenses. Hence, Gentamicin should not be used while wearing these lenses. The lenses should be removed before instillation of the drops and not reinserted earlier than 15 minutes after use.

5. Interaction with other medicinal products and other forms of interaction

Concurrent use with other potentially nephrotoxic or ototoxic drugs should be avoided. Prolonged corticosteroid therapy may be more likely to occur with concomitant use of anticholinergic: atropine and related compounds. Other phosphate-containing eye medications. Dexamethasone therapeutically efficacy may be reduced by phenytoin, phenobarbitone, ephedrine and rifampicin. Glucocorticoids may increase plasma salicylate clearance, ritanovir and cobicistat may decrease dexamethasone clearance resulting in increased effects.

6. Pregnancy and Lactation

It should only be used when considered essential by physician and only if the anticipated benefit outweighs the potential risk.

7. ***Effects on ability to Drive and use Machines***

Effects on ability to drive and use machine is Not relevant.

8. Undesirable effect

This medication may temporarily sting or burn for a minute or two when first applied. If this continues or becomes bothersome, inform your doctor. Notify your doctor immediately if you develop: a skin rash, burning/irritation/swelling/itching/redness/pain in or around the eyes or ears. If using for your eyes, notify your doctor of: vision changes. If using for your ears, stop using this medication and tell your doctor immediately if any of these unlikely but serious side effects occur: hearing loss, ringing in the ear, dizziness, loss of coordination. If you notice other effects not listed above, contact your doctor.

9. Overdose

Dexamethasone: Overdose is unlikely to occur as are single-dose units. Excess Drops may be wiped away with a clean tissue. Gentamicin: Haemodialysis and peritoneal dialysis will

aid the removal from blood but the former is probably more efficient. Calcium salts given intravenously have been used to counter the neuromuscular blockade caused by gentamicin

5. Pharmacological Properties

5.1 Pharmacodynamics Properties

Pharmacotherapeutic Group: Corticosteroids and aminoglycoside antibiotic in combination
ATC Code: S01CA01

Dexamethasone: Very potent and highly selective glucocorticoid. Long acting. Causes marked, pituitary adrenal suppression, but fluid retention and hypertension are not a problem. It meets any emergency with intensified potency and strikingly rapid corticosteroid action, thus ensuring speedy reversal of the situation in the patients favour.

Gentamicin: It is an aminoglycoside antibiotic effective against both gram-positive and gram negative organisms. It is active alone but also as a synergistic companion with betalactum against pseudomonas, proteus, enterobacter, klebsiella, serratia.

5.2 Pharmacokinetic Properties

Dexamethasone: 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 a volume of distribution has been quoted as 0.58 l/kg. Over 60% of circulating steroids are excreted in the urine within 24 hours, largely as unconjugated steroid. Dexamethasone sodium phosphate is rapidly converted to dexamethasone within the circulation. Up to 77% of dexamethasone is bound to plasma proteins, the mean plasma half-life 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.

Gentamicin: Topical application of gentamicin can result in some systemic absorption. Treatment of large areas can result in plasma concentrations of up to 1µg/ml.> 90% gentamicin is excreted in the urine by glomerular filtration.< 10% is bound to plasma protein.T½ = 2 - 3 hours in individuals with normal kidney function, but can be increased in cases of renal insufficiency.

5.3 Preclinical Safety Data

<u>Acute toxicity</u>

Antibiotic:

Investigations of the acute toxicity in various species have found no particular sensitivity.

Corticosteroid:

The LD50 within the first 7 days for dexamethasone after a single oral dose is 16 g/kg body weight in the mouse and 3 g/kg body weight in the rat. After a single subcutaneous administration, the LD50 within 7 days in the mouse is greater than 700 mg/kg body weight and about 120 mg/kg body weight in the rat. The values are reduced gradually over a period of 21 days, which is regarded as the consequence of severe infectious disease, caused by hormone-linked immune suppression.

Chronic toxicity

Antibiotic:

Studies on chronic toxicity after intramuscular administration to various animal species showed nephrotoxic and ototoxic effects at higher dosages.

Application to the eye:

Absorption is negligibly small after topical administration to the eye, so that systemic toxic effects can hardly be expected. Also refer to section 4.8 Undesirable Effects.

Corticosteroid:

There is no data on chronic human or animal toxicity. No corticosteroid-linked toxicity symptoms are known. Distinctive side effects can be expected after long-term therapy with doses in the range of or above the Cushing threshold (1.5 mg/day) (see Section 4.8).

Mutagenic and carcinogenic potential

Antibiotic:

No extensive mutagenicity tests are available for gentamicin. Previous investigations have been negative. There are no long-term animal studies available on potential carcinogenicity.

Corticosteroid:

The available study results on glucocorticoids do not provide any evidence that these substances possess clinically relevant genotoxic properties.

Reproduction toxicity

Antibiotic:

Gentamicin crosses the placenta and also passes into breast milk in low levels. Although there have been no reports about harmful effects of gentamicin, there is a potential danger of damage to the inner ear or kidneys of the foetus.

Corticosteroid:

In experiments in mice, rats, hamsters, rabbits and dogs, dexamethasone causes cleft palate and to a slight extent - other malformations. Disturbances in intrauterine growth have been observed.

6. Pharmaceutical Particulars

6.1 List of Excipients

Povidone (PVPK-30)
Disodium Edetate (Inj.)
Sodium Dihydrogen Phosphate Dihydrate
Anhydrous Disodium Hydrogen Phosphate
Sodium Metabisulfite
Polysorbate-80 (Tween-80)
Benzalkonium Chloride Solution
Water for Injections

6.2 Incompatibilities

Not applicable

6.3 Shelf Life

24 Months

Use the solution within 28 days after opening the container.

6.4 Special Precautions for Storage

Do not store above 30°C. Protect from light. Do not Freeze.

6.5 Nature and contents of container

A clear colourless to pale yellow colour clear solution filled in 10 ml sterile non transparent plastic dropper bottle with nozzle and white plastic cap. Such 1 dropper bottle packed in printed carton with packing insert

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 Authorization Holder and Manufacturing Site Addresses

7.1 Name and Address of Marketing Authorization Holder

Lincoln Pharmaceuticals Limited
Trimul Estate, Khatraj, Tal. Kalol,
Dist. Gandhinagar,

Gujarat, India.

7.2 Name and Address of Manufacturing Site(s)

Lincoln Parenteral Limited
11, Trimul Estate, Khatraj, Taluka: Kalol,
District: Gandhinagar Gujarat, India.

8 Marketing Authorization Number

TAN 22 HM 0415

9 Date of First Registration / Renewal of The Registration

21/09/2022

10 Date of Revision of the Text

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