SUMMARY PRODUCT CHARACTERISTICS (SPC)

DEXAMETHASONE AND GENTAMICIN EYE/EAR DROPS (Ivydexgent eye/ear drops)

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1. NAME OF MEDICINAL PRODUCT:
DEXAMETHASONE AND GENTAMICIN EYE DROPS
(Ivydexgent eye/ear drops)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Qualitative composition:
This product contains two APIs:
Dexamethasone phosphate (as dexamethasone sodium phosphate) BP
Gentamicin sulphate BP

Quantitative composition:
Dexamethasone (as dexamethasone phosphate) 0.1%$^{w}/_{v}$.
Gentamicin sulphate 0.3%$^{w}/_{v}$.

For full list of Excipients, see section 6.1

3. PHARMACEUTICAL FORM OF THE DRUG PRODUCT
EYE/EAR DROP
5ml clear colourless to slightly yellow solution

4. CLINICAL PARTICULARS
4.1 INDICATIONS
For the treatment of the external structures of the eye and its adnexa caused by susceptible bacteria. Such infections include conjunctivitis, keratitis, kerato-conjunctivitis, corneal ulcers, blepharitis and blepharo-conjunctivitis, acute meibomianitis, episcleritis and dacryocystitis. It may be used for the prevention of ocular infection after: removal of a foreign body, burns or lacerations of the conjunctiva; damage from chemical or physical agents and after ocular surgery. Also indicated for treatment of otitis externa.
For the treatment of swelling, itching, redness and irritation of the eyes and eye lids.

4.2 Posology and method of administration:
For use in the eye:
The normal dosage is 1-2 drops to be put in the affected eye up to 6 times a day or as directed by your doctor.
For use in the ear:
2 or 3 drops are usually put in the ear 3-4 times a day and at night or as directed by your doctor.
Do not touch your eye/ear with the dropper tip on the bottle as this may contaminate the drops.

4.3 Contraindications:

Should not be administered to patients with a known allergy to gentamicin or any of the ingredients, or other aminoglycosides. Evidence exists that gentamicin may cause neuromuscular blockade and is therefore contra-indicated in myasthenia gravis and related conditions. Perforation of the ear drum.

Use is also contraindicated in cases of:

• Epithelial herpes simplex keratitis.

• Vaccinia, varicella or other viral infection of cornea and conjunctiva.

• Fungal diseases of ocular structures

• In children, long-term, continuous corticosteroid therapy should be avoided due to possible adrenal suppression

4.4 Special warnings and pre cautions for use

The condition of the ear drum must always be checked before this medicinal product is prescribed. Avoid prolonged use. Prolonged use may lead to skin sensitization and the emergence of resistant organisms. Cross-sensitivity with other aminoglycoside antibiotics may occur. In severe infections, topical use of gentamicin should be supplemented with appropriate systemic antibiotic treatment. Irreversible toxic effects may result from direct contact of gentamicin with the middle and inner ear. This medicinal product must not be used if the integrity of the ear drum cannot be guaranteed. Serious adverse reactions including neurotoxicity, ototoxicity and nephrotoxicity have occurred in patients receiving systemic gentamicin therapy. Although these effects have not been reported following topical otic use of gentamicin, caution is advised when used concomitantly with systemic aminoglycosides.
Should be used cautiously in patients with glaucoma and be considered carefully in patients with family history of this disease.
This product contains phosphates which may lead to corneal deposits or corneal opacity when topically administered. It should be used with caution in patients presenting with compromised corneal and in instances where the patient is receiving polypharmacy with other phosphate containing eye medications.
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 installation of the drops, this especially advisable in children.

4.5 Interactions with other medicinal products and other forms of interactions

Potent diuretics such as ethacrynic acid and furosemide are believed to enhance any risk of ototoxicity whilst amphotericin B, cisplatin and cyclosporine and cephalosporin are potential enhancers of nephrotoxicity. Concurrent use with

other potentially nephrotoxic or ototoxic drugs should be avoided unless considered essential by the physician.
Neuromuscular blockade and respiratory paralysis have been reported in patients from the administration of aminoglycosides to patients who have received curare-type muscle relaxants during anaesthesia.
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.
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.
Therapeutic efficacy of dexamethasone may be reduced by phenytoin, phenobarbitone, ephedrine and rifampicin. Glucocorticoids may increase the need for salicylates as plasma salicylate clearance is increased.

4.6 Pregnancy and lactation
There are no proven cases of intrauterine damage caused by gentamicin. However, in common with most drugs known to cross the placenta, usage in pregnancy should only be considered in life-threatening situations where expected benefits outweigh possible risks. In the absence of gastrointestinal inflammation the amount of gentamicin ingested from the milk is unlikely to result in significant blood levels in breast-fed infants.
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 this product during pregnancy should be avoided.
Topically applied dexamethasone is not recommended in breastfeeding mothers, as it is possible that traces of the dexamethasone may enter the breast milk.

4.7 Effects on ability to drive and use machines
Patients should be advised that the use of Dexamethasone and gentamicin in the eye may cause transient blurring of vision. If affected, patients should not drive or operate machinery until vision has cleared.
4.8 Undesirable effects
There are no modern clinical studies available that can be used to determine the frequency of undesirable effects due to topical application of gentamicin. Therefore, all the undesirable effects listed are classed as ‘frequency unknown’
<u>Eye Disorders:-</u>
Local sensitivity; blurred vision, eye irritation, burning sensation, stinging sensation, itching (eye pruritus)
<u>Ear & Labyrinth Disorder:-</u>
Local sensitivity; ototoxicity; vestibular disorder; hearing loss.
<u>Skin & Subcutaneous tissue Disorders:-</u>
Burning sensation, stinging, itching (pruritus); dermatitis.
<u>Renal & Urinary Disorders:-</u>

Nephrotoxicity; acute renal failure.
In the event of irritation, sensitivity or super-infection, treatment should be discontinued and appropriate therapy instituted.

Prolonged treatment with corticosteroids in high dosage is, rarely, associated with sub-capsular cataract. In diseases which cause thinning of the cornea or sclera, perforations of the globe have been known to occur. In addition, optic nerve damage and visual acuity and field defects may arise following long term use of this product.
The administration of phosphates contained in Ivydexgent eye/ear drops has caused isolated cases of corneal deposits or corneal opacity when administered in patients presenting with compromised cornea.
The systemic effects of corticosteroids are possible with excessive use of steroid eye drops.

4.9 Overdose

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.

5.0 Pharmacological properties

5.1 Pharmacodynamic properties

Gentamicin is a mixture of antibiotic substance produced by the growth of micromonospora purpurae. It is bactericidal with greater antibacterial activity than streptomycin, neomycin or kanamycin. Gentamicin exerts a number of effects on cells of susceptible bacteria. It affects the integrity of the plasma membrane and the metabolism of RNA, but it's most important effect is inhibition of protein synthesis at the level of the 30s ribosomal subunit.
Dexamethasone is a highly potent and long acting-glucocorticoid. It has an approximately seven times greater anti-inflammatory potency than prednisolone. The actions of corticosteroids are mediated by the binding of the corticosteroid molecules to receptor molecules located within sensitive cells. Corticosteroids receptors are present in human trabecular meshwork cells and in rabbit iris ciliary body tissues. Corticosteroids will inhibit phosphate A2 thereby preventing the generation of substances which mediate inflammation, for example, prostaglandins. Corticosteroids also produce a marked. Though transient, lymphocytopenia. This depletion is due to redistribution of the cells, the T lymphocytes being affected to a greater degree than the B lymphocytes. Lymphokine production is reduced, as is the sensitivity of macrophages to activation by lymphokines.
Corticosteroids also retard epithelial regeneration, diminish post-inflammatory neo-vascularisation and reduce towards normal levels the excessive permeability of inflamed capillaries.

5.2 Pharmacokinetic properties

Gentamicin is not readily absorbed from the gastro-intestinal tract. Gentamicin is 70-85% bound to plasma albumin following administration and is excreted 90% unchanged in urine. The half-life for its elimination in normal patients is 2 to 3 hours. Effective plasma concentration is 4-8ug/ml.
The volume for distribution (VD) is 0.3 l/kg
The elimination rate constant is;
0.02Hr-1 for anuric patients*
0.03Hr-1 normal
*Therefore in those with anuria care must be exercised
When given topically to the eye, dexamethasone is absorbed 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. Dexamethasone sodium phosphate is rapidly converted to dexamethasone within the circulation. Upto 77% of dexamethasone is bound to plasma proteins, mainly albumin. This percentage, unlike cortisol, remains practically unchanged with increasing steroid concentrations. The mean plasma half-life of dexamethasone is 3.6 ± 0.9h.
Tissue distribution studies in animals show high 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.

5.3 Preclinical safety data

Pre-clinical safety data does not add anything of further significance to the prescriber.
The use of corticosteroids, including Dexamethasone sodium phosphate topically and its derivatives in ophthalmology is well established. Little relevant toxicology has been reported, however, the breadth of clinical experience confirms its suitability as a topical ophthalmic

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Name of ingredient	**Reference**	**Amount per 5ml**	**Function/Reason For inclusion.**
Disodium edetate	BP	5mg	Chelating agent
Sodium phosphate monobasic	BP	15mg	Buffering agent
Sodium phosphate dibasic	BP	160mg	Buffering agent
Creatinine	BP	20mg	Solubilizer
Benzalkonium chloride	BP	0.5mg	Preservative

Sodium metabisulphite	BP	25mg	Antioxidant
Water for injection	BP	Quantity Sufficient to volume	Solvent

6.2 Incompatibilities
Gentamicin is pharmaceutically incompatible with amphotericin, cephalosporins, erythromycin, heparin, penicillins, sodium bicarbonate and sulphadiazine sodium.

6.3 Shelf life
Unopened shelf-life is 24 months.
Opened shelf-life 28 days.
But the patient is advised to discard any remaining drops after the prescribed course of treatment.

6.4 Special precautions for storage
Store in a cool place (below 25° C) away from light. Keep out of reach of children

6.5 Nature and contents of container
5ml low density polyethylene bottles with a polypropylene spiked cap.

6.6 Special precautions for disposal

No special requirement

7 MARKETING AUTHORISATION HOLDER

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8 MARKETING AUTHORISATION NUMBER

Registration number: NAFDAC REG NO. 04 – 4169

9 DATE OF FIRST REGISTRATION/ RENEWAL OF REGISTRATION

10 DATE OF REVISION OF TEXT
November 2020-11-25

11 DOSIMETRY (IF APPLICABLE) Not Applicable

12 INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUICALS (IF APPLICABLE) Not applicable