1. NAME OF THE MEDICINAL PRODUCT

STADEX® - PLUS EYE DROPS

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5ml contains Dexamethasone Sodium Phosphate 0.1% $^{w}/_{v}$ + Chloramphenicol 0.5% $^{w}/_{v}$.

(For a full list of excipients, see section 6.1).

3. PHARMACEUTICAL FORM

Eye Drop

4. Clinical particulars

4.1 Therapeutic indications

Allergic and inflammatory infections but not purulent forms of conjunctivitis and blepharitis. Inflammation of the anterior uvea (iritis, iridocylitis) of exogenous or endogenous origin. Scleritis, episcleritis and myositis.
Post-operative anti -exudative treatment after eye surgery of any kind.
Chloramphenicol is a broad spectrum antibiotic indicated in both adults and children for the treatment of bacterial conjunctivitis caused by chloramphenicol susceptible organisms including: Escherichia coli, Haemophilus influenzae, Staphylococcus aureus, Streptococcus haemolyticus, Morax-axenfeld, Klebsiella/Enterobacter species and others.

4.2 Posology and method of administration

One drop 3-5 times daily , but in severe cases up to one drop hourly may be administered.
Do not touch your eye with the dropper on the bottle as this may contaminate the drops.

4.3 Contraindications

Injuries and ulcerating conditions of the cornea, especially those of viral Origin (herpes simplex, vaccina), purulent infections of the conjunctiva and eyelids, tuberculosis affections mycosis and glaucoma.

4.4 Special warnings and precautions for use

Dexamethasone Sodium Phosphate

For ocular use only, not for injection. 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.

Chloramphenicol

Chloramphenicol is absorbed systemically from the eye and toxicity has been reported following chronic exposure.

Bone marrow hypoplasia, including aplastic anaemia and death, has been reported following topical use of chloramphenicol. Whilst the hazard is a rare one, it should be borne in mind when assessing the benefits expected from the use of the compound. Where chloramphenicol eye drops are used on a long-term or intermittent basis, it may be advisable to perform a routine blood profile before therapy and at appropriate intervals thereafter to detect any haemopoietic abnormalities.

In severe infections the topical use of chloramphenicol should be supplemented by appropriate systemic treatment.

Prolonged use of chloramphenicol eye drops should be avoided as it may increase the likelihood of sensitisation and emergence of resistant organisms. If any new infection appears during the treatment, the antibiotic should be discontinued and appropriate measures taken. Chloramphenicol should be reserved for use only in infections for which it is specifically indicated.

Chloramphenicol Eye Drops does not provide adequate coverage against Pseudomonas aeruginosa and Serratia marcescens.

Do not use for more than 5 days without consulting a doctor.

Medical advice should be sought if there is no improvement in the condition after 2 days or if symptoms worsen at any time.

Patients should be referred to their doctor if any of the following apply:

- Disturbed vision
- Severe pain within the eye
- Photophobia
- Eye inflammation associated with a rash on the scalp or face
- The eye looks cloudy
- The pupil looks unusual
- Suspected foreign body in the eye

Patients should also be referred to their doctor if any of the following in his/her medical history apply:

- Previous conjunctivitis in the recent past
- Glaucoma
- Dry eye syndrome
- Eye surgery or laser treatment in the last 6 months
- Eye injury
- Current use of other eye drops or eye ointment
- Contact lens use

Soft contact lenses should not be worn during treatment with chloramphenicol eye drops due to absorption of the preservative onto the lens which may cause damage to the lens. It is recommended that all types of contact lenses be avoided during ocular infections.

The packaging will convey the following information:
• If symptoms do not improve within 48 hours talk to your doctor
• Seek further immediate medical advice at any time if symptoms worsen
• Do not use if you are allergic to chloramphenicol or any of the ingredients
Phenylmercuric nitrate is irritating to the skin. Topical application to eyes has been associated with mercurialentis and atypical band keratopathy.

4.5 Interaction with other medicinal products and other forms of interaction

Dexamethasone Sodium Phosphate

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.

Chloramphenicol

The concomitant administration of Chloramphenicol with other drugs liable to depress bone marrow function should be avoided.

4.6 Pregnancy and Lactation

Dexamethasone Sodium Phosphate

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.

Chloramphenicol

The safety of topical use of chloramphenicol in pregnancy and lactation has not been established.
Chloramphenicol may be absorbed systemically following the use of eye drops and may cross the placenta and appear in breast milk. Therefore this product is not recommended for use during pregnancy and lactation.
Fertility
No fertility data are available

4.7 Effects on ability to drive and use machines

Dexamethasone Sodium Phosphate

Installation of this eye drop may cause transient blurring of vision. Warn patients not to drive or operate hazardous machinery until vision is clear.

4.8 Undesirable effects

Dexamethasone Sodium Phosphate

Administration of Dexamethasone sodium phosphate 0.1% w/v Eye drops to the eye may rarely cause stinging, burning, redness or watering of the eyes. 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 dexamethasone eye 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.

Chloramphenicol

Eye disorders
Transient irritation, burning, stinging and sensitivity reactions such as itching and dermatitis.
Immune system disorders
Hypersensitivity reactions including angioedema, anaphylaxis, urticaria, fever, vesicular and maculopapular dermatitis.
Blood and lymphatic system disorders
Bone marrow depression and rarely aplastic anaemia has been reported following topical use of chloramphenicol. Whilst the hazard is a rare one, it should be borne in mind when assessing the benefits expected from the use of this compound.

4.9 Overdose

Dexamethasone

Products with dexamethasone are usually in single dose unit therefore overdose is unlikely to occur

Chloramphenicol

Accidental ingestion of the eye drops is unlikely to cause systemic toxicity due to the low content of the antibiotic in the product. If irritation, pain, swelling, lacrimation or photophobia occur after undesired eye contact, the exposed eye(s) should be irrigated for at least 15 minutes. If symptoms persist after this, an ophthalmological examination should be considered.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamics properties

Dexamethasone Sodium Phosphate

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.

Chloramphenicol

Pharmacotherapeutic group: Antibiotics for Systemic use : ATC Code: S01AA01

Chloramphenicol is a broad spectrum antibiotic with bacteriostatic activity and is effective against a wide range of gram-negative and gram-positive organisms including Haemophilus influenzae, Streptococcus pneumoniae, Staphylococcus aureus, Streptococcus viridans, Moraxella species and Enterobacteriaceae, the main pathogens responsible for acute bacterial conjunctivitis. Chloramphenicol exerts its antibacterial effect by reversibly binding to bacterial ribosomes thereby inhibiting bacterial protein synthesis.

5.2 Pharmacokinetic properties

Dexamethasone Sodium Phosphate

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. 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

Chloramphenicol

Chloramphenicol is an extremely well established antibiotic and the successful use of the eye drops is well documented. Chloramphenicol is found in measurable amounts in the aqueous humour following local application to the eye.

5.3 Preclinical safety data

Dexamethasone Sodium Phosphate

The use of corticosteroids, including Dexamethasone sodium phosphate 0.1 % w/v Eye

drops 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 agent.

Chloramphenicol
Nothing of relevance which is not included in other sections of the SPC.

6.0 PHARMACEUTICALPARTICULARs

6.1 List of Excipients

Thiomersal
Citric Acid
Sodium Citrate
Hypromellose E4m Premium
Polyethylene Glycol (Peg400)
Water For Injection To

6.2 Incompatibilities

None have been reported or are known

6.3 Shelf life

24 Months

6.4 Special precautions for storage

Store below 30^{o}C in tight container Protect from light and moisture. Replace cap immediately after use. Discard after 28days of opening the bottle.

6.5 Nature and contents of container and special equipment for use, administration or implantation

Stadex® - Plus Eye Drops is available in sterile Lupolen containing 5ml of the sterile drops

6.6 Special precautions for disposal and other handling

No special requirements.

7 APPLICANT/MANUFACTURER

Drugfield Pharmaceuticals Limited
Lynson Chemical Avenue Km38,
Lagos-Abeokuta Expressway
Sango-Otta, Ogun State, Nigeria
Tel: +2348033513989
Email:Info@drugfieldpharma.com