SUMMARY OF PRODUCT CHARACTERISTICS

1. Name of the medicinal product:
Dexamethasone Sodium Phosphate Ophthalmic Solution USP

2. Qualitative and quantitative composition:
Composition:

Dexamethasone Sodium Phosphate USP		
Eq. to Dexamethasone Phosphate		0.1%w/v
Benzalkonium Chloride Solution	USP	0.02% v/v
(As preservative)		
Aqueous base		q.s.

3. Pharmaceutical form:
Eye drops, solution.
Clear colourless liquid.

4. Clinical particulars:
4.1 Therapeutic indications
Dexamethasone Sodium Phosphate Ophthalmic Solution USP are indicated for inflammatory conditions of the anterior segment of the eye, such as marginal keratitis, stromal oedema in keratitis, anterior uveitis, episcleritis (if NSAIDs are contraindicated or insufficient), scleritis, acute phase of severe allergic conjunctivitis not responding to standard therapy.

4.2 Posology and method of administration
Posology
Adults (including the elderly)

The usual dose in adults, including the elderly, is 1 drop, 4 to 6 times daily.

In severe conditions, the treatment can be used more frequently at first (1 drop every hour), and then reduced to 1 drop every 4 hours as the eye inflammation subsides. Dexamethasone sodium phosphate dosage should be progressively reduced.

Paediatric population
Use of Dexamethasone Sodium Phosphate Ophthalmic Solution USP 0.1% w/v Eye Drops, solution in children and adolescents must be restricted. No data on safety and efficacy are available for children aged less than 2 years. In children, long-term continuous corticosteroid therapy should be avoided due to possible adrenal suppression.

Method of administration
Ocular use.

4.3 Contraindications
Hypersensitivity to the active substance or to any of the excipients listed .Use is contra-indicated in herpes simplex and other viral diseases of the cornea and conjunctiva, fungal disease, ocular tuberculosis, untreated purulent infections, patients with a history of acute epithelial herpes simplex keratitis or hypersensitivity to any component of the preparation.

4.4 Special warnings and precautions for use
For ocular use only. Not for injection into the eye.

Care should be taken to ensure that the eye is not infected before Dexamethasone Sodium Phosphate Ophthalmic Solution USP are used.

In those diseases causing thinning of the cornea or sclera, perforations have been known to occur with the use of topical corticosteroids.

Caution is also necessary when used in conjunction with antiviral therapy in the treatment of stromal keratitis or uveitis and use of periodic slit-lamp microscopy.

Corticosteroids may reduce resistance to and aid in the establishment of bacterial, viral and fungal infections and mask the clinical signs of infections, preventing recognition of ineffectiveness of the antibiotic. In such cases antibiotic therapy is mandatory. Fungal infection should be suspected in patients with persistent corneal ulceration who have been or are receiving these drugs, and corticosteroids therapy should be discontinued if fungal infection occurs.

This medicinal 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 cornea and in instances where the patient is receiving polypharmacy with other phosphate-containing eye medications .

Topical corticosteroids should not be used for longer than one week except under ophthalmic supervision. Prolonged use of topical ophthalmic corticosteroids may result in ocular hypertension and/or glaucoma, with damage to the optic nerve, reduced visual acuity, visual field defects and posterior subcapsular cataract formation. In patients receiving prolonged ophthalmic corticosteroid therapy, intraocular pressure and the lens should be checked routinely and frequently, particularly in patients with a history or presence of glaucoma. The dose of anti-glaucoma medication may need to be adjusted in these patients. Prolonged use may also increase the hazard of secondary ocular infections. Topical ophthalmic corticosteroids may slow corneal wound healing.

Cushing's syndrome and/or adrenal suppression associated with systemic absorption of ophthalmic 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.

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 instillation of the drops. (This blocks the passage of drops via the naso-lacrimal duct to the wide absorptive area of the nasal and pharyngeal mucosa. It is especially advisable in children.)
Paediatric population
In children, long-term, continuous corticosteroid therapy should be avoided due to possible adrenal suppression.

4.5 Interaction with other medicinal products and other forms of interaction:
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.
The following drug interactions are possible, but are unlikely to be of clinical significance, following the use of Dexamethasone Sodium Phosphate Ophthalmic Solution USP.

The 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.

CYP3A4 inhibitors (including ritanovir 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.

4.6 Fertility, pregnancy and lactation:
Pregnancy
There are no or limited amount of data from the use of dexamethasone eye drops in pregnant women. Studies in animals have shown that topically applied steroids can be absorbed systemically and can cause abnormalities of foetal development in pregnant animals . Although the relevance of these findings to human beings has not been established, the use of Dexamethasone Sodium Phosphate Ophthalmic Solution USP 0.1% w/v Eye Drops during pregnancy should be avoided.

Breastfeeding
Systemically administered corticosteroids appear in human milk in quantities that could affect the child being breastfed. However, when instilled topically, systemic exposure is low. It is unknown whether dexamethasone is excreted in human milk. A risk to the suckling child cannot be excluded. A decision must be made whether to discontinue breastfeeding or to discontinue/abstain from dexamethasone therapy taking into account the benefit of breastfeeding for the child and the benefit of therapy for the woman.

4.7 Effects on ability to drive and use machines:
Dexamethasone Sodium Phosphate Ophthalmic Solution USP have no or negligible influence on the ability to drive and use machines; however, instillation of eye drops may cause transient blurring of vision. Warn patients not to drive or operate hazardous machinery until vision is clear.

4.8 Undesirable effects:
The following undesirable effects are classified according to the following convention: very common (1/10), common (1/100 to <1/10), uncommon (1/1,000 to <1/100), rare (1/10,000 to <1/1000), very rare (<1/10,000), or not known (cannot be estimated from the available data). Within each frequency grouping, undesirable effects are presented in decreasing order of seriousness.

Ocular disorders:
- Very common (>1/10): intraocular pressure increased (after 2 weeks of treatment).
- Common (>1/100, <1/10): ocular discomfort after instillation, irritation, burning, eye pruritus and blurred vision. These symptoms are mild and transient with no consequences.
- Uncommon (>1/1,000, <1/100): signs and symptoms of allergic or hypersensitive reactions can occur. The following corticoid specific undesirable effects can occur: delay in healing, risk of posterior subcapsular cataract formation, opportunist infections and glaucoma.
- Very rare (<1/10,000, including isolated reports): conjunctivitis, eyelid oedema, corticoid-induced uveitis, keratitis, corneal thinning, corneal oedema and ulcerations. Cases of corneal calcification have been reported in association with the use of phosphate containing eye drops in some patients with significantly damaged corneas. Due to the steroid component, in diseases causing thinning of the cornea or sclera, there is a higher risk for perforation especially after topical long treatments.

General disorders and administration site conditions:
- Uncommon (>1/1,000, <1/100): after long treatment posology, systemic absorption can occur with an inhibition of the adrenal function.

4.9 Overdose
Overdose is unlikely to occur as Dexamethasone Sodium Phosphate Ophthalmic Solution USP are single-dose units. Excess Dexamethasone Sodium Phosphate Ophthalmic Solution USP may be wiped away with a clean tissue.

5. Pharmacological properties
5.1 Pharmacodynamic properties
Pharmacotherapeutic group: Corticosteroids, plain, ATC code: S01 BA01
Dexamethasone is a highly potent and long-acting glucocorticoid. It has an approximately 7 times greater anti-inflammatory potency than prednisolone, another commonly prescribed corticosteroid.
The actions of corticosteroids are mediated by the binding of the corticosteroid molecules to receptor molecules located within sensitive cells. Corticosteroid receptors are present in human trabecular meshwork cells and in rabbit iris ciliary body tissue.

Corticosteroids will inhibit phospholipase A2 thereby preventing the generation of substances which mediate inflammation, for example, prostaglandins. Corticosteroids also produce a marked, though transient, lymphocytopaenia. 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.

The actions of corticosteroids described above are exhibited by dexamethasone and they all contribute to its anti-inflammatory effect.

5.2 Pharmacokinetic properties

Absorption

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.

Distribution

Tissue distribution studies in animals show 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.

Biotransformation

Dexamethasone sodium phosphate is rapidly converted to dexamethasone within the circulation. Up to 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.

Elimination

Dexamethasone also appears to be cleared more rapidly from the circulation of the foetus and neonate than in the mother; plasma dexamethasone levels in the foetus and the mother have been found in the ratio of 0.32:1.

5.3 Preclinical safety data

Repeat dose topical ocular safety studies with dexamethasone in rabbits have shown systemic corticosteroid effects. Such effects are considered to be unlikely when dexamethasone eye drops are used as recommended.

Dexamethasone was clastogenic in the in vitro human lymphocyte assay and in vivo in the mouse micronucleus assay at doses in excess of those obtained following topical application. Conventional carcinogenicity studies with dexamethasone have not been performed.

Dexamethasone has been found to be teratogenic in animal models. Dexamethasone induced abnormalities of foetal development including cleft palate, intra-uterine growth retardation and effects on brain growth and development.

There are no other preclinical data of relevance to the prescriber which are additional to that included in other sections of the SPC.

6. Pharmaceutical particulars:

6.1 List of excipients:

Sodium Dihydrogen Phosphate
Sodium Phosphate
Sodium Metabisulphite
Disodium Edetate
Hydroxypropyl methyl cellulose

Benzalkonium Chloride Solution
Polysorbate 80
Purified water

6.2 Incompatibilities
None known. In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 Shelf life
24 months.

6.4 Special precautions for storage
Keep out of reach of children.
Keep in cool dark place.

6.5 Nature and contents of container
10 ml sterile opaque plastic bottle with cap packed in a carton with pack insert.

6.6 Special precautions for disposal and other handling
No special requirements

7. Marketing authorisation holder
M/s. LinKabs Pharmaceuticals Ltd.,
42 Ziks Avenue,
Fegge- Onitsha Box 10239,
Onitsha, Nigeria