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APR 24 1997

**REVIEW AND EVALUATION OF PHARMACOLOGY AND TOXICOLOGY DATA  
NDA 20-803**

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**ORIGINAL SUMMARY**

**SUBMISSION DATE:** January 31, 1997  
**CENTER RECEIPT DATE:** February 3, 1997  
**REVIEWER RECEIPT DATE:** February 10, 1997  
**DRAFT REVIEW COMPLETE:** April 18, 1997

**SPONSOR:** Pharmos Corporation, 2 Innovation Drive, Alachua, Florida 32615  
**DRUG:** Loteprednol etabonate 0.2%

**FORMULATION:** Loteprednol etabonate 0.2% ophthalmic suspension is a sterile aqueous suspension packaged in multiple use dropper bottles. The formulation for this drug product is shown in the table below.

**Loteprednol etabonate 0.2%**

Component	Concentration (mg/mL)
Loteprednol etabonate.	
Glycerin, USP.	
Povidone, USP	
Tyloxapol, USP	
Benzalkonium Chloride Solution.	
Edetate Disodium Dihydrate, USP	
Purified Water, USP	qs to 1.0 mL
Hydrochloric Acid,	adjust pH
Sodium Hydroxide.	adjust pH

**PROPOSED INDICATION:** Treatment of the signs and symptoms of seasonal allergic conjunctivitis.

**RELATED DRUGS/INDs/NDAs:** The sponsor has submitted NDA 20-583 for loteprednol etabonate 0.5%.

**20-803**

**RECOMMENDED DOSAGE:** According to the proposed package labeling, 1 drop should be instilled into the affected eye(s) 4 times daily. Assuming a drop size of 50 uL and both eyes being affected, each patient will instill 400 uL of loteprednol etabonate 0.2% each day. A dose of 400 uL/day will contain 0.8 mg/day or 0.016 mg/kg/day (16 ug/kg/day) based on a 50 kg body weight.

**BACKGROUND INFORMATION:** Loteprednol etabonate is a corticosteroid with anti-inflammatory activity. The drug exhibits glucocorticoid actions with no detectable mineralocorticoid actions. Although corticosteroids offer the broadest treatment for the signs and symptoms of allergic conditions, their use is associated with several undesirable side effects, such as increased intraocular pressure in susceptible individuals, increased incidence of posterior subcapsular cataracts, and increased susceptibility to eye infections. Loteprednol etabonate was designed to address some of these untoward effects. In contrast to other steroids, which like prednisolone have a ketone group in the  $\beta$  side chain attached to the 17 carbon, loteprednol etabonate has an ester group. The ester group is cleaved by esterases to produce a compound which lacks glucocorticoid activity, an action which should decrease adverse effects.

In December 1988, the sponsor submitted The sponsor developed loteprednol etabonate 0.5%, Lotemax®, under this IND and submitted NDA 20-583 for this drug product in March 1995. Lotemax® was not approved due to deficiencies in the chemistry and clinical sections. The Pharmacology/ Toxicology section of NDA 20-583 was reviewed by David A. Shriver, Ph.D.; Dr. Shriver recommended approval of Lotemax®. The nonclinical Pharmacology/Toxicology section of NDA 20-583 has been referenced to support NDA 20-803.

**APPEARS THIS WAY  
ON ORIGINAL**