CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:
64-134

MEDICAL REVIEW

PATIENT SELECTION

Subjects of either sex and any race will be selected from an established database of noninstitutionalized individuals with a history of allergic conjunctivitis. A log will be kept of all patients screened for entry and those patients that are enrolled into the study.

Inclusion Criteria

1. Be 18 years of age or older.
2. Be able and willing to follow instructions.
3. Be able and willing to make the required study visits.
4. Manifest a successful ocular allergen challenge, inducing at least 2+ itching and 2+ hyperemia (redness) bilaterally at Visits 1 and 2.
5. Best corrected visual acuity of at least 20/100 in both eyes.
6. Have a positive history of allergy to grasses, animal dander, weeds, or trees. Positive skin tests, prior positive reactions to allergen challenge or verbal patient report consistent with allergy will constitute positive history.
7. Women of child bearing potential must have a negative pregnancy test at Visit 1 and must agree to use an acceptable mechanical (i.e., IUD, diaphragm with spermicide, condom with spermicide) or hormonal (i.e., oral, injectable or implantable) contraceptive for the duration of the study. Women are considered of childbearing potential unless they are surgically sterile (i.e., have undergone a tubal ligation or tubal section or have had a hysterectomy) or have been post menopausal for at least 2 years (i.e., have not had a menstrual cycle for at least 2 years).
8. Subjects must be able and willing to give consent.

Exclusion Criteria

1. Contraindications to the use of the study medication(s).
2. Known sensitivity or allergy to the study drug(s) or their components.
3. Known allergic reaction that is unresponsive to corticosteroids or non-steroidal anti-inflammatory drugs (NSAIDS).
4. Presence of any significant illness that could be expected to interfere with the study, particularly any autoimmune disease, e.g., rheumatoid arthritis.
5. Presence of bacterial or viral ocular infection.
6. Presence of blepharitis, follicular conjunctivitis, iritis, or preauricular lymphadenopathy.
7. Presence of mucous discharge, excess lacrimation, or burning as symptoms of ocular disease.
8. Evidence of dry eye demonstrated by slit lamp examination.
9. Manifestation of signs and symptoms of clinically active allergic conjunctivitis (> 1+ hyperemia and/or the presence of any itching) at the initial, baseline eye examination of each visit (Visits 1, 2).
10. Subject administration of ocular medications of any kind, including tear substitutes; or systemic medication that may interfere with a normal vasodilatory response or with normal lacrimation for an appropriate wash-out period prior to the start of the study and for the duration of the study (i.e., NSAIDS, anti-histamines, etc. within 72 hours, corticosteroids within 7 days, mast cell stabilizers within 14 days).
11. Ocular surgery or laser surgery within 6 months of start of study.
12. Contact lenses worn 3 days prior to or during study period.
13. Participation in a clinical trial or use of an investigational drug or device within the last 30 days.

Reviewer's Comments: *Acceptable.*

STATISTICAL ANALYSIS The primary analysis for efficacy will consist of a change from baseline comparison (Visit 3-Visit 2) of the conjunctival hyperemia and itching responses of TobraDex and placebo groups. The Visit 3 response will initially focus on the 6 hour challenge data. Safety assessments (e.g., visual acuity, IOP, adverse events) will be compared between the two treatment groups as appropriate.

Sample size for this pilot study was restricted arbitrarily to 60 subjects (12 subjects per loading regimen) to obtain estimates of magnitude of effect and variability for the definitive study. Although the study is likely to be under-powered and not able to achieve 80% power to detect a 0.5 unit mean change between treatment groups, significant differences may be noted.

Reviewer's Comments: *The study should attempt to determine the dosing regimen necessary to elicit a 1 unit change in itching and a 1 unit change in redness.*

Procedure	**Visit 1** (Day 0)	**Visit 2** (Day 7)	**Visit 3** (Day 21)
Informed Consent	X		
Demographics	X		
Inclusion/Exclusion Criteria	X	X	X
Medical/Surgical History	X	X	X
Urine Pregnancy (females only)	X		
Ophthalmic Exam: Visual Acuity & Slit Lamp Biomicroscopy	X	X	X
Randomization		X	
Ocular Signs and Symptoms of Allergic Conjunctivitis	X	X	X
Intraocular Pressure		X	X
Allergan Challenge	X	X	X
Photograph		X	
Dispense Medication			X
Recover Medication			X
Exit Form	X	X	X

[1]Evaluation of itching at 3, 5, and 10 minutes; evaluation of hyperemia at 10, 20, and 30 minutes after allergen challenge

[2]Intraocular pressure to be measured immediately following 30 minutes evaluation

[3]Allergen challenge to be performed 3 hours after drug administration and repeated 6 hours after drug administration

[4]Photographs taken immediately after 10 minute evaluation from the 6 hour challenge

[5]To be completed for those patients who don't qualify for randomization

Reviewer's Comments: *At least 2 of the evaluations for itching and redness (hyperemia) should overlap in time. It is recommended that itching be evaluated at 5, 10 and 15 minutes.*