CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-770

MEDICAL REVIEW

Medical Officer's Review of NDA 21-770
Labeling Review # 3

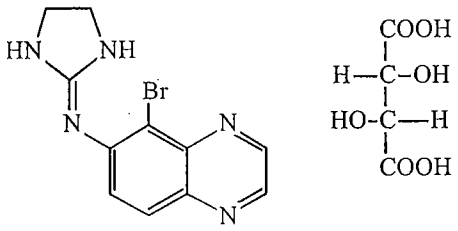
NDA 21-770
Medical Officer's Review

Submission: 8/03/05
Submission: 8/18/05
Review Completed: 8/18/05

Proposed Tradename: Alphagan P

Established Name: brimonidine tartrate ophthalmic solution, 0.1%

Chemical Structure:



Formula $C_{11}H_{10}BrN_5 \cdot C_4H_6O_6$

Sponsor: Allergan, Inc.
2525 Dupont Drive
P.O. Box 19534
Irvine, CA 92623-9534

Pharmacologic Category: Alpha 2-agonist

Proposed Indication: Reduction of intraocular pressure (IOP)

Dosage Form and Route of Administration: Ophthalmic solution for topical ocular administration

Submitted:

The following comments are from the DMETS review signed August 12, 2005:

A. GENERAL COMMENTS

1. We note that the preservative for this product bears the tradename "Purite®". We ask that you define Purite® in terms of its ingredients where it appears throughout your labels and labeling.

Reviewer's comments:

Purite® is a "stabilized oxychloro complex." Defining Purite® within the labeling will provide no additional beneficial information.

2. DMETS is aware of postmarketing reports of inadvertent oral administration of Alphagan resulting in hospitalization of pediatric patients. DMETS recommends the addition of a prominent statement on container labels and carton labeling of "Alphagan" products that these product are for use only in the eye. Alternatively (or additionally), DMETS recommends that an eye pictorial appear on those labels and labeling.

Reviewer's comments:

The cases referenced are children who accidentally ingested the medication not cases in which drug was mis-administered; it is unlikely that an eye pictorial or label statement would prevent accidental ingestion.

3. DMETS recommends that the statement, "New Product Strength" appears on product labels and labeling for a period of time not to exceed six months.

Reviewer's comments:

The proposed drug product is bioequivalent to the currently marketed product. There is no safety or efficacy issue related to substitution of these products.

4. When preparing product labeling, please ensure that the expression of strength is well differentiated from the expression of strength of the existing Alphagan P product. DMETS recommends the use of contrasting colors, boxing, or some other means to differentiate the product strengths.

Reviewer's comments:

The boxes for these products do differ in color. The Alphagan P 0.15% box top is in purple, while the Alphagan P 0.1% box top is in green. Even if one drug was inadvertently substituted for the other, these drugs are bioequivalent and have the same safety and efficacy profile.

5. According to the Division's Project Manager, the sponsor has proposed a separate package insert for the lower strength product. DMETS does not

recommend two separate package inserts for the two different strengths as this may cause confusion and error. For example, practitioners may not be aware of the two different strengths if only one strength is listed and/or they may think that the products are not indicated or dosed similarly. Traditionally, a combined package insert is used for different strengths of the same active ingredient.

Reviewer's comments:

A combined package insert will be used for both products (Alphagan P 0.15% and Alphagan P 0.1%).

10 Page(s) Withheld

_____ Trade Secret / Confidential

✓ Draft Labeling

_____ Deliberative Process

Withheld Track Number: Medical- 1

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