CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

22-369

CHEMISTRY REVIEW(S)

NDA 22-369
Bimatoprost Ophthalmic Solution 0.03%
Allergan, Inc.
Supporting Document: NDA 21-275 (Lumigan®)
NDA Received 27th June 2008
PDUFA Date: December 27, 2008
Reviewer. Shrikant Pagay

Recommendation on Approvability from Quality perspective: This NDA has provided sufficient information to assure identity, strength, purity, and quality of the drug product. The labels have adequate information as required. However, a recommendation from the Office of Compliance on the site acceptability has not been made as of the date of this review. Therefore, from the CMC perspective, this NDA is not recommended for approval until the site acceptability is established.

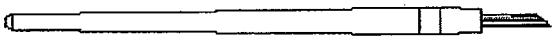
Description of the Drug Product: Refer to the same drug (NDA 21-275) approved on March 16, 2001for a different indication.
Bimatoprost ophthalmic solution 0.03% is proposed to be applied to the skin of the upper eyelid margin at the base of the eyelashes using the accompanying sterile disposable applicators. Bimatoprost is a prostamide structurally similar to other approved prostaglandin – dinoprost and latanoprost but differs in having an amide group in the chemical structure (described in the Label section). The proposed drug product is a clear, isotonic, colorless, sterile solution. The same solution was approved in NDA 21-275 under the trade name Lumigan® for lowering intraocular pressure (IOP) when instilled directly to the eye in patients with elevated IOP. The proposed indication for this NDA is improving the prominence of natural eyelashes as measured by increases in growth (length), fullness (thickness) and darkness (intensity). From CMC consideration the 2 drug products solution (NDA 21-275 and NDA 22-369) are identical with the exception of color of the container cap described under container closure system and labeling section for the proposed indication. Therefore, this review covers only those sections in which the 2 drug products differ from each other.

Manufacturing Facilities:
No changes were made in manufacturing and control facilities than the ones accepted by compliance for the approved NDA 21-275. However, the proposed facility inspection request (EER) was submitted on 17th July 2008 since NDA 21-275 was approved several years ago in 2001.

Container Closure:
The proposed drug product will have — cap whereas Lumigan has turquoise cap. The difference is that the proposed drug product cap contains —— to render color from turquoise to —. One additional change made in the primary packaging component is a disposable sterile applicator required for the administration of bimatoprost solution to the skin of the upper eyelid margin. The approved solution is administered by a dropper. b(4)

The container closure system for the sterile applicator is a ——— ——— tray with a ———lid. The applicators are sterilized using a ——— The secondary packaging is a retail paperboard unit carton containing six sterile applicator packages with 10 applicators per package for a total of 60 applicators (a one month supply). As shown in Figure 1, the sterile, single-use per eye disposable applicator is intended to apply bimatoprost solution 0.03% to the upper eyelid margin. It comprises ——— handle with an attached tuft made from multiple ——— The tuft is configured to optimize product application to the upper eyelid margin. b(4)

Figure 1: Applicator



Label:

Tradename is Pending.

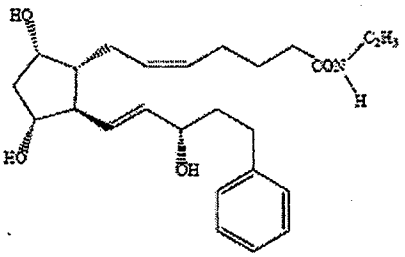
Dosage Forms and Strength

——— b(4)

Recommend "Bimatoprost Ophthalmic Solution 0.3 mg/mL"

DESCRIPTION

TRADENAME™ (bimatoprost solution) 0.03% is a synthetic prostamide analog. ——— Its chemical name is (Z)-7-[(1R,2R,3R,5S)-3,5-Dihydroxy-2-[(1E,3S)-3-hydroxy-5-phenyl-1-pentenyl]cyclopentyl]-5-N-ethylheptenamide, and its molecular weight is 415.58. Its molecular formula is $C_{25}H_{37}NO_4$. Its chemical structure is: b(4)



Bimatoprost is a powder, which is very soluble in ethyl alcohol and methyl alcohol and slightly soluble in water. TRADENAME™ is a clear, isotonic, colorless, sterile solution with an osmolality of approximately 290 mOsmol/kg.

Contains: Active: bimatoprost 0.03% (0.3 mg/mL); Preservative: benzalkonium chloride 0.05 mg/mL; Inactives: sodium chloride; sodium phosphate, dibasic; citric acid; and purified water. Sodium hydroxide and/or hydrochloric acid may be added to adjust pH. The pH during its shelf life ranges from 6.8 - 7.8.

Recommend to delete ——— *from the description section.* b(4)

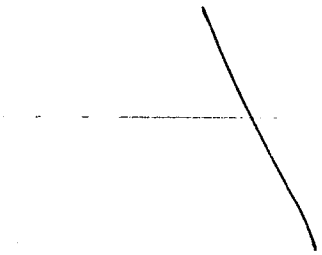
HOW SUPPLIED/STORAGE AND HANDLING
TRADENAME™ (bimatoprost solution) 0.03% is supplied sterile in opaque white low density polyethylene dispenser bottles and tips with —— polystyrene caps accompanied by 60 sterile, disposable applicators: b(4)

The proposed statement: is 3 mL in a 5 mL bottle NDC 0023-

Recommend: Each 5 mL bottle contains 3 mL bimotoprost solution.

Storage: TRADENAME™ should be stored at 2° to 25°C (36° to 77°F).

Applicator Box label:



b(4)

The directions for how to use this product from the applicator box label text is enlarged and listed below;

1 Page(s) Withheld

_____ Trade Secret / Confidential (b4)

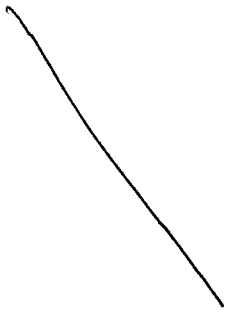
__X__ Draft Labeling (b4)

_____ Draft Labeling (b5)

_____ Deliberative Process (b5)

Withheld Track Number: Chemistry- 1

Carton Label:



b(4)

The prominence of establishment name with respect to the trade name meets regulatory criteria.

Proposed Shelf Life:

The stability data support a 24 month expiration dating when packaged in the proposed package configuration and stored at 2 °C to 25 °C (36 °F – 77 °F).

Acceptable based on the NDA 21-275 and S-014 and S-015 stability data.

Establishment Inspection: Pending

Establishment Evaluation Report: Pending

3 Page(s) Withheld

X Trade Secret / Confidential (b4)

_____ Draft Labeling (b4)

_____ Draft Labeling (b5)

_____ Deliberative Process (b5)

Withheld Track Number: Chemistry- 2

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/s/

Shrikant Pagay
12/15/2008 03:47:33 PM
CHEMIST

Norman Schmuff
12/16/2008 10:48:53 AM
CHEMIST

Memorandum

To: Elaine Morefield, Div Dir, ONDQA

From: Stephen Miller, PAL, ONDQA

Date: December 19, 2008

Regarding: NDA 22-369 – Bimatoprost Solution 0.03%

The acceptability of the manufacturing facilities was the remaining CMC issue that needed to be resolved before approval of NDA 22-369.

The EES report (attached below) now shows an Overall Recommendation of Acceptable (Dated Dec 19, 2008), so this NDA is recommended for approval from the CMC perspective.

ESTABLISHMENT EVALUATION REQUEST

SUMMARY REPORT

Application : NDA 22369/000
Sponsor: ALLERGAN INC
Org Code : 520
NO CITY, , XX
Priority : 6P
Brand Name : BIMATOPROST SOLUTION 0.03%
Stamp Date : 27-JUN-2008
Estab. Name:
PDUFA Date : 27-DEC-2008
Generic Name: BIMATOPROST SOLUTION 0.03%
Action Goal :
Dosage Form: (SOLUTION)
District Goal: 28-OCT-2008
Strength : 0.03%

FDA Contacts:	N. PUGLISI	Project Manager (HFD-520)	301-796-0791
	S. PAGAY	Review Chemist	301-796-1429
	N. SCHMUFF	Team Leader	301-796-1454

Overall Recommendation: ACCEPTABLE on 19-DEC-2008by S. ADAMS (HFD-325) 301-796-3193

Establishment : CFN : 1643525 FEI : 1643525
ALLERGAN INC
8301 MARS DR
WACO, TX 767126578
DMF No: AADA:

Responsibilities: FINISHED DOSAGE MANUFACTURER

Profile : SNI OAI Status: NONE
Last Milestone: OC RECOMMENDATION
Milestone Date: 29-JUL-08
Decision : ACCEPTABLE
Reason : DISTRICT RECOMMENDATION

Establishment : CFN : 9616651 FEI : 3002806285
ALLERGAN PHARMACEUTICALS IRELAND
CASTLEBAR ROAD
WESTPORT, , EI

Responsibilities: FINISHED DOSAGE STABILITY TESTER

Profile : CTX OAI Status: NONE

Last Milestone: OC RECOMMENDATION

Milestone Date: 19-DEC-08

Decision : ACCEPTABLE

Reason : DISTRICT RECOMMENDATION

Establishment : CFN : [redacted] FEI : [redacted]

[redacted]

DMF No: AADA: b(4)

Responsibilities:

[redacted]

ESTABLISHMENT EVALUATION REQUEST

SUMMARY REPORT

Profile : CSN OAI Status: NONE
Last Milestone: OC RECOMMENDATION
Milestone Date: 19-DEC-08
Decision : ACCEPTABLE
Reason : DISTRICT RECOMMENDATION

Establishment : CFN : [redacted] FEI :

[redacted]

DMF No: AADA:

b(4)

Responsibilities: [redacted]

Profile : [redacted] OAI Status: NONE
Last Milestone: OC RECOMMENDATION
Milestone Date: 16-OCT-08
Decision : ACCEPTABLE
Reason : DISTRICT RECOMMENDATION

Establishment : CFN : [redacted] FEI : [redacted]

[redacted]

DMF No: AADA:

b(4)

Responsibilities: [redacted]

Profile : [redacted] OAI Status: NONE
Last Milestone: OC RECOMMENDATION
Milestone Date: 24-JUL-08
Decision : ACCEPTABLE
Reason : DISTRICT RECOMMENDATION

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Stephen Paul Miller
12/19/2008 03:09:27 PM
CHEMIST
EES shows overall acceptable

Elaine Morefield
12/19/2008 03:10:31 PM
CHEMIST