

CNC

Division of Anti-inflammatory, Analgesic and Ophthalmic Drugs
Review of Chemistry, Manufacturing, and Controls

NDA #: 21-114

REVIEW # 1

DATE REVIEWED: 12/29/99 (revised 1/20/00)

<u>SUBMISSION TYPE</u>	<u>DOCUMENT DATE</u>	<u>CDER DATE</u>	<u>ASSIGNED DATE</u>
Original pre-submission	5/25/99	5/27/99	10/15/99
Amendment	10/1/99	10/4/99	10/25/99
Amendment	12/13/99	12/15/99	
Amendment	12/17/99	12/20/99	
Amendment	12/20/99	12/21/99	

NAME & ADDRESS OF APPLICANT:

Alcon Laboratory, Inc.
6201 South Freeway
Ft Worth, TX 76134

DRUG PRODUCT NAME

Proprietary: Betaxon
Established: Levobetaxolol
Code Name #: AL 1577A, Formulation 93492
Chem. Type/Ther. Class: 2P

PHARMACOL. CATEGORY:

Anti-hypertensive, Beta-adrenergic receptor blocker

DOSAGE FORM:

Suspension

STRENGTHS:

0.5%

ROUTE OF ADMINISTRATION: topical/ocular (1-2 drops daily)

DISPENSED:

☒ Rx ☐ OTC

CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA AND WEIGHT:

Common Name

Levobetaxolol Hydrochloride

(Levobetaxolol hydrochloride is the S-isomer of the well-known and well characterized compendial [USP and Ph.Eur.] drug betaxolol hydrochloride).

USAN / INN Name

Levobetaxolol Hydrochloride

Chemical Name

(S)-1-[p-[2-(cyclopropylmethoxy)ethyl]phenoxy]-3-(isopropylamino)-2-propanol hydrochloride
or:

2-propanol, 1-[4-[2-(cyclopropylmethoxy)ethyl]phenoxy]-3-[(1-methylethyl)amino]-,
hydrochloride, (S)

NDA 21-114

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C1CC1COCCc2ccc(OCC[C@H](O)CNCC(C)C)cc2.Cl
$$\text{C}_{18}\text{H}_{29}\text{NO}_3 \cdot \text{HCl}$$

343.89

116209-55-3

(S) - Betaxolol Hydrochloride

AL-1577A

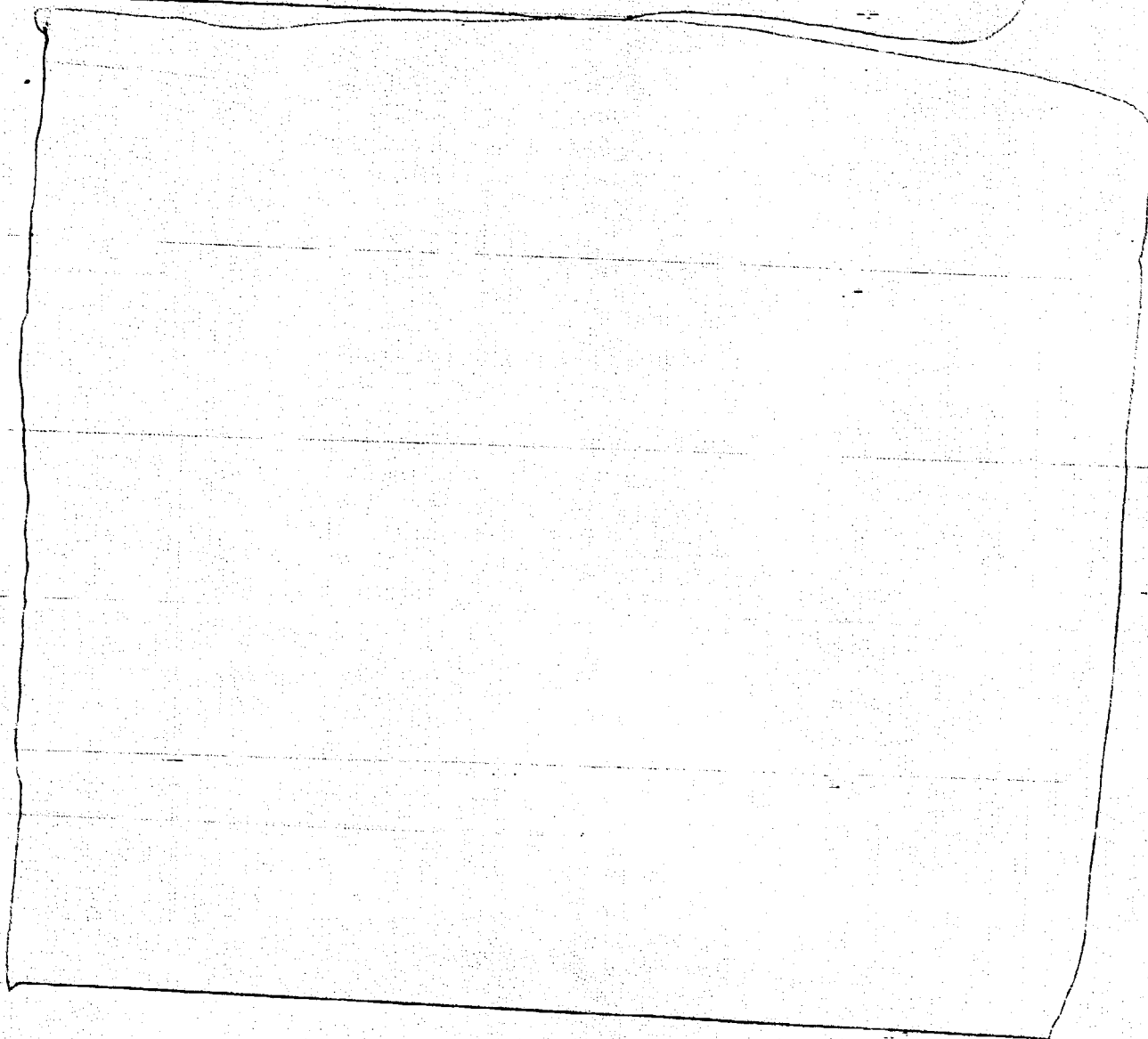
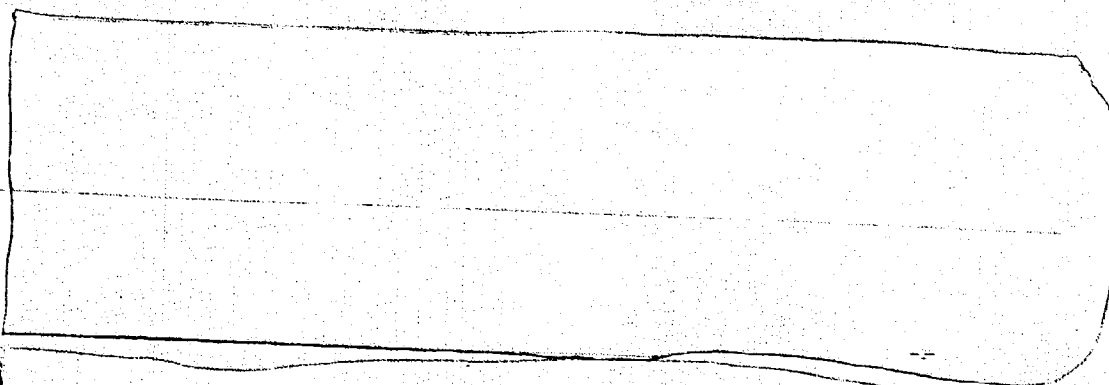
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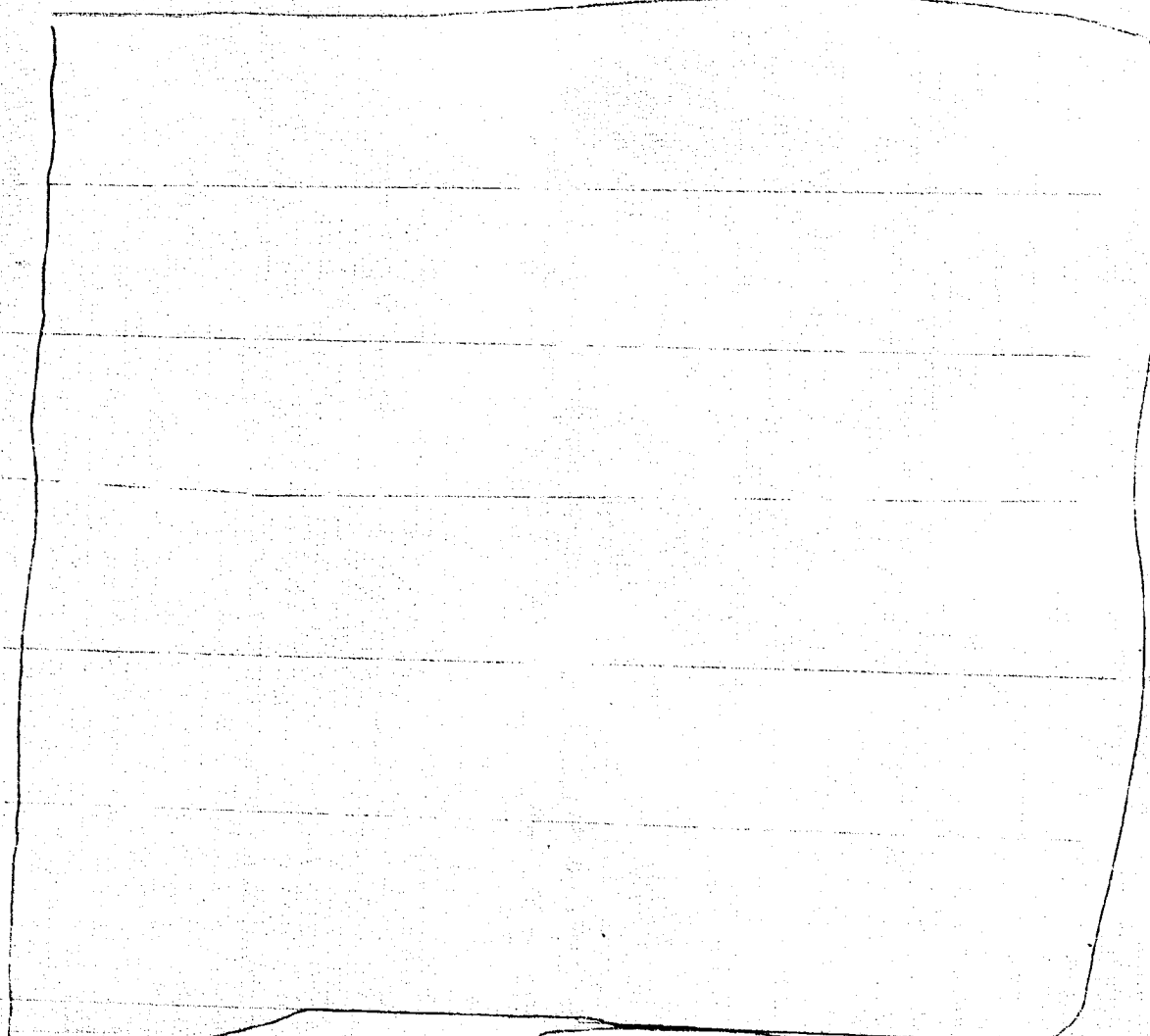
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Levobetaxolol hydrochloride
Alcon Laboratories

NDA 21-114

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Orig. NDA 21-114
HFD-550/Division File
HFD-550/Tso
HFDD-550/Gorski
HFD-830/CWChen
HFD-550/Boyd
HFD-550/Mukherjee
HFD-550/Ng
HFD-550/Chambers
HFD-550/Fenselau

APPEARS THIS WAY
ON ORIGINAL

/S/

Chemist, HFD-550/830-
Su C. Tso, Ph.D.

/S/

Linda Ng, Ph.D.
Chemistry Team Leader, HFD-550

1/24/00

Division of Anti-inflammatory, Analgesic and Ophthalmic Drugs
Review of Chemistry, Manufacturing, and Controls

NDA #: 21-114

REVIEW # 1

DATE REVIEWED: 27-JAN-00

<u>SUBMISSION TYPE</u>	<u>DOCUMENT DATE</u>	<u>CDER DATE</u>	<u>ASSIGNED DATE</u>
Original pre-submission	25-MAY-99	27-MAY-99	02-JUN-99
Original submission	08-SEP-99	10-SEP-99	17-SEP-99
Amendment	01-OCT-99	04-OCT-99	17-OCT-99
Amendment	15-OCT-99	18-OCT-99	25-OCT-99
Amendment	13-DEC-99	15-DEC-99	21-DEC-99
Amendment	17-DEC-99	20-DEC-99	28-DEC-99
Amendment	24-JAN-00	27-JAN-00	27-JAN-00

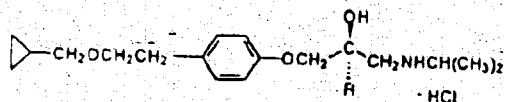
NAME & ADDRESS OF APPLICANT:

Alcon Laboratory, Inc.
6201 South Freeway
Ft Worth, TX 76134

DRUG PRODUCT NAME

Proprietary: Betaxon
Established: Levobetaxolol
Code Name/#: CAS-116209-55-3; AL 1577A
Chem. Type/Ther. Class: 2P

PHARMACOL. CATEGORY: Anti-hypertensive; Beta-adrenergic receptor blocker
DOSAGE FORM: Suspension
STRENGTHS: 0.5%
ROUTE OF ADMINISTRATION: Topical/ocular (1-2 drops; twice daily)
DISPENSED: ☒ Rx ☐ OTC
CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA AND WEIGHT:



$C_{18}H_{29}NO_3 \cdot HCl$
M.W.: 343.89

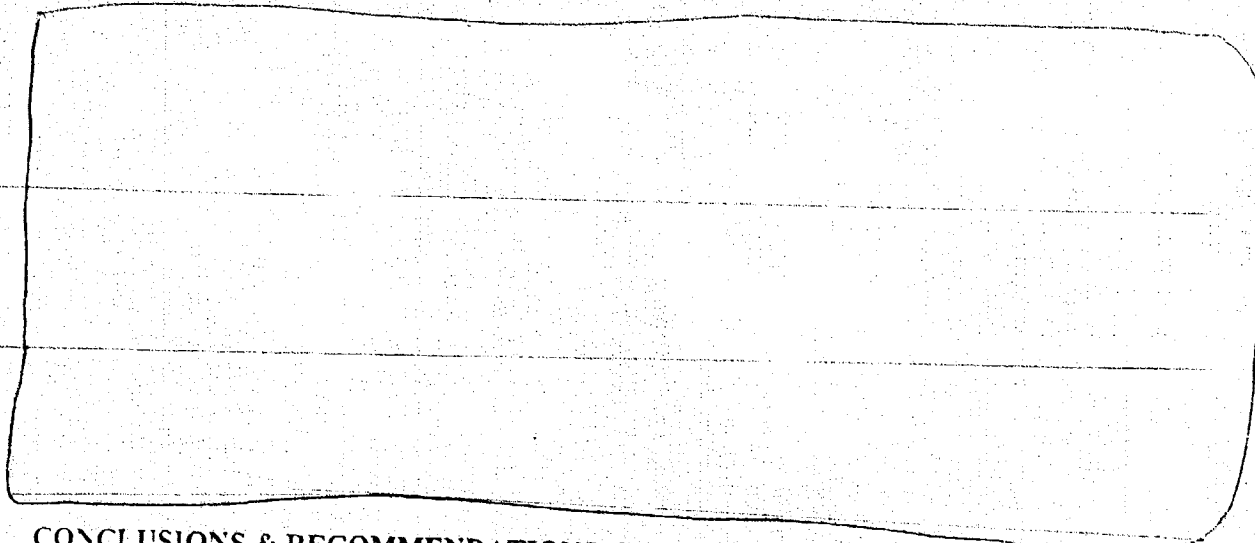
LEVOBETAXOLOL HCl

(S)-1-[4-(2-Cyclopropylmethoxy)phenoxy]-3-
[(1-methylethyl)amino]-2-propanol hydrochloride

SUPPORTING DOCUMENTS:

DMF
DMF
DMF

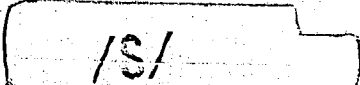


RELATED DOCUMENTS:Chemistry Reviews of IND 

CONCLUSIONS & RECOMMENDATIONS: Based on a review of chemistry, manufacturing and control issues that pertain only to the drug substance levobetaxolol, the application can be approved. Additional satisfactory reviews of the drug product BETAXON and microbiology issues as well as a satisfactory cGMP inspection will be needed to complete the review process.

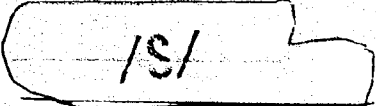
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Orig. NDA 21-114
HFD-550/Division File
HFD-550/CSO/L.Gorski
HFD-550/Chem/ A.Fenselau
HFD-550/TeamLdr./L.Ng
HFD-550/Pharm./L.Gorski
HFD-550/MO/W.Boyd
HFD-550/Dep.Div.Dir./W.Chambers
HFD-830/Div.Dir.DNDCIII/C.-w.Chen
filename: n21114ds.doc

 /S/

1/27/00

Allan Fenselau, Review Chemist, HFD-550

 /S/

1/27/00

Linda Ng, Chemistry Team Leader HFD-550

APPEARS THIS WAY
ON ORIGINAL

New Drug Application Review
Levobetaxolo Hydrochloride
Alcon Laboratories

NDA 21-114

1

Division of Anti-inflammatory, Analgesic and Ophthalmic Drugs
Review of Chemistry, Manufacturing, and Controls

NDA #: 21-114

REVIEW # 2

DATE REVIEWED: 1/28/99

<u>SUBMISSION TYPE</u>	<u>DOCUMENT DATE</u>	<u>CDER DATE</u>	<u>ASSIGNED DATE</u>
Original pre-submission	5/25/99	5/27/99	10/15/99
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Amendment	12/13/99	12/15/99	
Amendment	12/17/99	12/20/99	
Amendment	12/20/99	12/21/99	
Amendment	1/24/00	1/28/00	

Amendment dated 1/20/00 is a response to the deficiencies sent to Alcon on 1/4/00 by fax. This report covers the review of the amendment dated 1/24/00 that are related to the drug product only.

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Levobetaxolol Hydrochloride

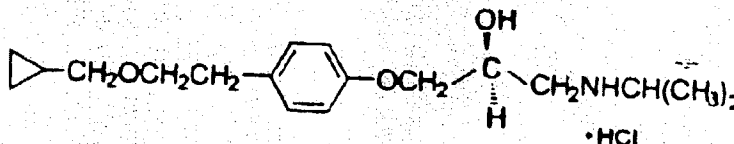
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or:

2-propanol, 1-[4-[2-(cyclopropylmethoxy)ethyl]phenoxy]-3-[(1-methylethyl)amino]-, hydrochloride, (S)

Structural Formula



Molecular Formula

$C_{18}H_{29}NO_3 \cdot HCl$

Molecular Weight:

COMMENTS:

Microbiologist's concern is adequate according to microbiology reviewer (refer to micro reviews). All manufacturing facilities are in cGMP compliance.

CONCLUSIONS & RECOMMENDATIONS:

The application is recommended for approval from the chemistry, manufacturing, and control standpoint. The application may be approved with expiration dates of 24 month for the trade size and 18 month for the professional sample when stored at 4 - 25°C

cc: --
Orig. NDA 21-114
HFD-550/Division File
HFD-550/Tso
HFDD-550/Gorski
HFD-830/CWChen
HFD-550/Boyd
HFD-550/Mukherjee
HFD-550/Ng
HFD-550/Chambers
HFD-550/Fenselau

APPEARS THIS WAY
ON ORIGINAL

/S/ [Signature]
Chemist, HFD-550/830
Su C. Tso, Ph.D.

/S/ [Signature]
1/28/00
Linda Ng, Ph.D.
Chemistry Team Leader, HFD-550