CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: 20-830

CHEMISTRY REVIEW(S)

DEC 19 1997

DIVISION OF PULMONARY DRUG PRODUCTS

Review of Chemistry, Manufacturing, and Controls

NDA #: 20-830 **CHEM.REVIEW #:** 3 **REVIEW DATE:** 15-Dec-97

SUBMISSION TYPE	DOCUMENT DATE	CDER DATE	ASSIGNED DATE
ORIGINAL	21-FEB-97	21-FEB-97	28-FEB-97
AMENDMENT	17-JUN-97	18-JUN-97	25-JUN-97
AMENDMENT	31-JUL-97	01-AUG-97	07-AUG-97
	ADDRESSED IN THIS REVIEW		
AMENDMENT N(BC)	13-NOV-97	14-NOV-97	19-NOV-97
AMENDMENT N(BC)	26-NOV-97	28-NOV-97	05-Dec-97
AMENDMENT N(BL)	25-NOV-97	26-NOV-97	08-DEC-97
AMENDMENT N(BC)	14-OCT-97	15-OCT-97	21-OCT-97
AMENDMENT N(BL)	11-DEC-97	12-DEC-97	16-DEC-97

NAME & ADDRESS OF APPLICANT: Merck Research Laboratories
Sumneytown Pike
West Poimt, PA 19486

DRUG PRODUCT NAME

Proprietary:	Singular Chewable Tablets
Nonproprietary/USAN:	montelukast sodium
Code Name/#:	MK-476
Chem.Type/Ther.Class:	1 S

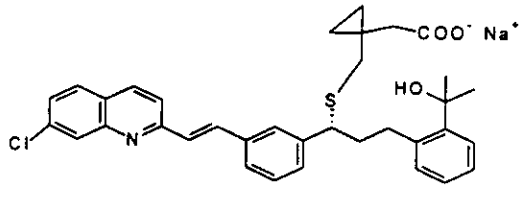
ANDA Suitability Petition/DESI/Patent Status: N/A

PHARMACOL.CATEGORY/INDICATION: Treatment of asthma (leukotriene antagonist)

DOSAGE FORM: tablet, chewable
STRENGTHS: 5 mg
ROUTE OF ADMINISTRATION: oral, one tablet per day
DISPENSED: __X__ Rx _____ OTC

CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOL.WT:

Sodium 1-[[[(R)-*m*-[(E)-2-(7-chloro-2-quinolyl)vinyl]-α-[*0*-(1-hydroxy-1-methylethyl)phenethyl]benzyl]thio]methyl]cyclopropaneacetate



Molecular Formula: $C_{35}H_{35}ClNNaO_3S$
Molecular Weight: 608.18

NDA 20-830

From a chemistry and manufacturing basis, the application may be approved. The approval letter should include a statement that the validation of the methods by our laboratories has not been completed, and should problems be found in the methods, the applicant will cooperate to solve the problems. The allowed expiry for the drug product should be stated in the approval letter as 24 months based on submitted data for HDPE bottles and for blisters. The package insert should be modified as indicated in the attached draft letter.

cc:
Orig. NDA 20-830
HFD-570/Division File
HFD-570/JLeak/GPoochikian
HFD-570/CSO
HFD-820/JGibbs

R/D Init by /S/ 12/19/97

/S/

John C. Leak, Review Chemist
filename: 20830B.NDA

OCT 15 1997

DIVISION OF PULMONARY DRUG PRODUCTS
Review of Chemistry, Manufacturing, and Controls

NDA #: 20-830 **CHEM.REVIEW #:** 1 **REVIEW DATE:** 01-OCT-1997

SUBMISSION TYPE	DOCUMENT DATE	CDER DATE	ASSIGNED DATE
ORIGINAL	21-FEB-97	21-FEB-97	28-FEB-97
	ADDRESSED IN THIS REVIEW		
AMENDMENT	17-JUN-97	18-JUN-97	25-JUN-97
AMENDMENT	31-JUL-97	01-AUG-97	07-AUG-97
AMENDMENT	23-SEP-97		

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West Poimt, PA 19486

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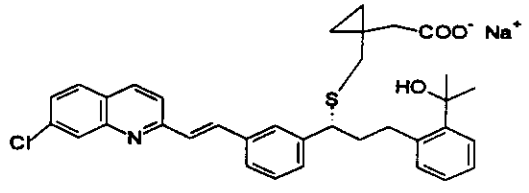

APPEARS THIS WAY
ON ORIGINAL

levels in the coated tablets should occur within a year of approval and presented to the Agency, based on results for production lots prepared at full scale.

CONCLUSIONS & RECOMMENDATIONS:
Deficiencies found in the following review should be sent to the applicant for correction. The project manager should forward to the applicant the items in the attached draft letter.

cc:
Orig. NDA 20-830
HFD-570/Division File
HFD-570/JLeak/
HFD-570/CSO /S/ 10/15/97
HFD-570/GPoochikian
HFD-570/Gibbs
R/D Init by:

/S/
John C. Leak, Review Chemist
filename: 20830A.NDA

APPEARS THIS WAY
ON ORIGINAL

JUN 18 1997

DIVISION OF PULMONARY DRUG PRODUCTS
Review of Chemistry, Manufacturing, and Controls

NDA #: 20-830 – **CHEM.REVIEW #:** 1 **REVIEW DATE:** 11-June-97

SUBMISSION TYPE	DOCUMENT DATE	CDER DATE	ASSIGNED DATE
ORIGINAL	21-FEB-97	21-FEB-97	28-FEB-97

NAME & ADDRESS OF APPLICANT: Merck Research Laboratories
Sumneytown Pike
West Poimt, PA 19486

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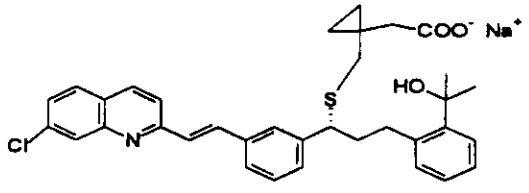

Molecular Formula: $C_{35}H_{35}ClNNaO_3S$
Molecular Weight: 608.18

RELATED DOCUMENTS (if applicable):
Supporting INDs & NDAs included above.

CONSULTS:

ENVIRONMENTAL ASSESSMENT:	requested 3/12/97; pending
METHODS VALIDATION:	requested 4/4/97; pending
ESTABLISHMENT INSPECTION:	requested 3/6/97; pending
NOMENCLATURE COMMITTEE:	requested 3/13/97; The Committee finds the proposed name unacceptable 3/27/97. Pending division decision regarding acceptance of proposed name.
PHARMACOLOGY REVIEW:	requested on artificial cherry flavor 5/16/97; pending

REMARKS/COMMENTS:
Proposed expiry:
for HDPE bottles and for blisters - 18 months based on submitted data for 12 months. Additional data is to be submitted with the proposal to extend the expiry. No data has been submitted on batches of drug product manufactured at the commercial manufacturing site.

CONCLUSIONS & RECOMMENDATIONS:
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cc:
Orig. NDA 20-830
HFD-570/Division File
HFD-570/JLeak/
HFD-570/CSO
HFD-570/GPoochikian

R/D Init by: /S/ 6/18/97

/S/

John C. Leak, Review Chemist
filename: 20830.NDA

APPEARS THIS WAY
ON ORIGINAL