CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: 20-830

ADMINISTRATIVE DOCUMENTS

APPENDIX II

MATERIAL SAFETY DATA SHEET (MSDS) FOR DRUG SUBSTANCE

MATERIAL SAFETY DATA SHEET

PRODUCT NAME: **MONTELUKAST SODIUM** **PAGE: 1 OF 8**
PLANT MSDS CODE: **BA-062** **Date: 11/96**

1. Chemical Product and Company Identification

Manufacturer----------	**MERCK SHARP AND DOHME (IRL) LTD.** **BALLYDINE, KILSHEELAN,** **CLONMEL, COUNTY TIPPERARY,** **IRELAND**
Emergency Telephone Number------	**051-601000 (Ireland)** **1-908-594-5555 (U.S.)**
Label Name----------	Montelukast Sodium
Chemical Name----------	[R-(E)]-1-[[[1-[3-[2-(7-chloro-2-quinolinyl)ethenyl]phenyl]-3-[2-(1-hydroxy-1-methylethyl)phenyl]propyl]thio]methyl] cyclopropaneacetic acid monosodium salt
Synonyms----------	(R)-1-[[1-(3-(2-(7-Chloro-2-quinolinyl) ethenyl)phenyl)-3-(2-(2-hydroxy-2-propyl) phenyl)propyl]thiomethyl]cyclopropane acetic acid sodium salt; MK-0476, L-706,631; Singulair(TM)
Material Statistical Number-----	2-02440
Material Product Number---------	Not available
Intended Use----------	Anti-asthmatic; Leukotriene D4 (LTD4) Antagonist.

2. Composition/Information on Ingredients

Component	Molecular Formula	Molecular Weight	CAS Number	Percent (%)
Montelukast Sodium	$C_{35}H_{35}ClNO_3SNa$	608.2	151767-02-1	100%

EC Label---------- Xi, R41

3. Hazards Identification

Appearance----------	Clean white to off white powder.
Emergency Overview----------	WARNING! Pharmaceutical active ingredient. Anti-asthmatic drug. Risk of serious damage to eyes. Mildly irritating to skin.

*** Continued on next page ***

Potential Health Effects--------	Practically non-toxic by ingestion. Mildly irritating to the skin. Severely irritating to the eyes.

4. First-Aid Measures

Eye Contact----------	In case of contact, immediately flush eyes with plenty of water for at least 15 minutes. Get medical attention immediately.
Skin Contact----------	In case of contact, immediately flush skin with plenty of water while removing contaminated clothing and shoes. Get medical attention if symptoms occur. Wash clothing before reuse. Thoroughly clean shoes before reuse.
Inhalation----------	Get medical attention immediately. If inhaled, remove to fresh air. If not breathing, give artificial respiration. If breathing is difficult, give oxygen.
Ingestion----------	Get medical attention if symptoms appear. Do NOT induce vomiting unless directed to do so by medical personnel. Never give anything by mouth to an unconscious person.
Note to Physicians----------	Not available

5. Fire-Fighting Measures

Flash Point ($^{o}C/^{o}F$)----------	Not applicable
Flash Point Test Method---------	Not applicable
Flammable Limits-LEL (%)--------	Not applicable
-UEL (%)--------	Not applicable
Autoignition Temperature ($^{o}C/^{o}F$)-	Not available
Oxidizing Properties----------	Not available
Combustibility Information------	Not available

*** Continued on next page ***

Dust Explosivity Information----	Tests show a minimum ignition energy between 10 and 30 milliJoules. At this energy level all plant and equipment should be grounded. The hazard from electrostatic discharges from dust clouds should be considered.
Shock Sensitivity----------	Not available
Fire/Explosion Hazards----------	Not available
Extinguishing Media----------	In case of fire, use water spray (fog), foam, dry chemical or CO_2.
Special Fire Fighting Procedures-	Fire fighters should don SCBA and protective clothing.
Hazardous Decomposition Products Resulting From a Fire----------	CO, CO_2, phosgene and oxides of nitrogen and sulphur may be released in a fire.

6. Accidental Release Measures

Personal Precautions----------	Immediately contact emergency personnel. Keep unnecessary personnel away. Use suitable protective equipment (Section 8). Follow all fire fighting procedures (Section 5).
Environmental Precautions-------	Avoid contact of spilled materials and runoff with soil and surface waterways.
Methods for Cleaning Up---------	If emergency personnel are unavailable, vacuum or carefully scoop up spilled materials and place in an appropriate container for disposal. Avoid creating dusty conditions.

For additional assistance in the U.S., CHEMTREC provides a toll-free Hotline for chemical emergencies regarding spills, leaks, exposure or accidents: 1-800-424-9300.

7. Handling and Storage

Handling----------	Avoid contact with skin and eyes. Do not ingest. Refrain from smoking or eating when handling. Wash thoroughly after use. Prevent product dust generation. If exposure is likely wear protective equipment (See Section 8).

*** Continued on next page ***

Storage---------- Store in a closed container in a cool, dry, well-ventilated location. Keep container closed when not in use. Protect from exposure to light and moisture.

Other---------- Avoid electrostatic charging of product by the following grounding measures: ground containers during filling and emptying; ground all conductive installation parts of filling equipment; avoid non-conductive layers on conductive supports.

8. **Exposure Controls/Personal Protection**

Exposure Guidelines

Component	Irish Occupational Exposure Limit (OEL)	OSHA Permissible Exposure Limit (PEL)	ACGIH Threshold Limit Value (TLV)	Merck Exposure Control Limit (ECL)
Montelukast Sodium	Not established	Not established	Not established	0.1 mg/m3 (8hr-TWA)

Engineering Controls

Ventilation---------- No special containment is required. Local exhaust ventilation should be provided.

Personal Protective Equipment

Eye/Face Protection---------- Safety glasses are required. Goggles, face shield or other full-face protection is required if potential exists for direct exposure to dust or aerosols.

Hand/Arm Protection---------- Latex gloves, or gloves providing greater protection, are required. Double latex gloves are recommended.

Respiratory Protection---------- An approved, properly fit tested, HEPA filtered cartridge respirator, or a respirator of greater protection, is required.

Additional Protective Equipment- Laboratory coat or work uniform is required. Disposable outer garments are required if there is the potential for contact with dust. Additional body garments should be used based upon the task being performed (e.g., sleevelets, apron, gauntlets).

*** Continued on next page ***

PRODUCT NAME: MONTELUKAST SODIUM
PLANT MSDS CODE: BA-062

PAGE: 5 OF 8
Date: 11/96

9. Physical and Chemical Properties

Appearance	Clean white to off white powder
Odour/Threshold Level (ppm)	No odour
pH	9.4-10.2
Boiling Point/Range ($^{o}C/^{o}F$)	Not applicable
Melting Point/Range ($^{o}C/^{o}F$)	275.9^{o}F (135.5^{o}C)
Solubility in water	Greater than 100 mg/ml at approximately 25^{o}C
Partition Coefficient (Kow)	The partition coefficient, expressed as Log P, is 2.3.
Specific Gravity (Water=1)	(bulk density)
Vapour Density (Air=1)	Not applicable
Vapour Pressure (mmHG @ $^{o}C/^{o}F$)	Not applicable
Volatile Components (% w/w)	None

10. Stability and Reactivity

Stability	Photolabile, hygroscopic
Conditions to Avoid	Exposure to light or moisture
Incompatibilities	Not available
Hazardous Polymerizations	Will not occur
Hazardous Decomposition Products	

11. Toxicological Information

Primary Route(s) of Entry	Inhalation: Yes Ingestion: No Skin Contact: No

*** Continued on next page ***

Toxicity Data

TEST	SPECIES	ROUTE	RESULT
Acute	Rat	Oral	LD50 Greater than 5000 mg/kg
Acute	Mouse	Oral	LD50 Greater than 5000 mg/kg
Irritation	Rabbit	Dermal	Mildly irritating
Irritation	Rabbit	Ocular	Severely irritating

Effects of Acute Exposure

Eye Contact---------- Severely irritating to the eyes.

Skin Contact---------- Mildly irritating to the skin.

Inhalation---------- No data available

Ingestion---------- Practically non-toxic by ingestion. In clinical trials, MK-0476 has been well tolerated, producing only mild adverse reactions. Adverse reactions considered possibly drug-related included headache, facial flushes, diarrhea, abdominal discomfort, sleepiness, light-headedness, eye twitching, nasal congestion and transient elevations in liver enzymes and bilirubin. The anticipated clinical dose is expected to range between 10 and 50 mg/day.

Effects of Chronic Exposure----- Montelukast sodium is a drug being developed for the treatment of asthma. In subacute and chronic studies minimal toxicity has been observed. Findings have been confined primarily to the slight, but transient increases in liver enzymes in rats only, and gastrointestinal tract distension by gas production attributable to the detergent effect of the compound. Occasional post-dosing salivation has also been noted. In reproductive and developmental toxicity studies in rats and rabbits, evidence of fetotoxicity and decreased fertility and fecundity were only observed at dosages toxic to adult animals. MK-0476 was negative in a battery of genotoxicity assays.

Carcinogen Designation---------- Not listed as a carcinogen by OSHA, IARC, or NTP.

Medical Conditions Aggravated by Exposure-- Not available

*** Continued on next page ***

12. Ecological Information

Environmental Fate---------- The partition coefficient, expressed as Log P, is 2.3. The compound degrades very rapidly in aqueous media under natural light.

Environmental Effects---------- The compound is considered to be moderately toxic.

LC50	Daphnia Magna, 48 hrs.	Greater than 1.5 mg/l
LC50	Fathead minnow, 96 hrs.	Greater than 1.5 mg/l
LC50	Rainbow trout	4.47 mg/l
EC10	ASRIT	Greater than 1.5 mg/l
EC50	Microtox(TM)	Greater than 1.5 mg/l

13. Disposal Considerations

Waste Disposal Information------ Dispose of or treat all spill residues including contaminated soils following all applicable regulations.

14. Transport Information

Shipping Description

U.S. DOT---------- Not Regulated, Drugs or Medicines, NOI

IATA/ICAO---------- Not Regulated, Drugs or Medicines, NOI

IMO---------- Not Regulated, Drugs or Medicines, NOI

ADR-RID---------- Not available

15. Regulatory Information

U.S. Federal Regulations-------- Not available

International Regulations------- Not available

State Regulations---------- This material Safety Data Sheet is written in compliance with the following Irish Legislation: The Safety, Health and Welfare at Work Act 1989 and The European Communities (Classification, Packaging, Labelling and Notification of Dangerous Substances) Regulations, 1994.

*** Continued on next page ***

16. Other Information

Date Prepared----------	June 1996
Last Revision Date----------	November 1996
MSDS Co-ordinator----------	1-908-423-7926 Merck & CO, Inc. One Merck Drive P.O. Box 100, WS2F-48 Whitehouse Station, NJ 08889-0100 USA

Disclaimer: While this information and recommendations set forth are believed to be accurate as of the date hereof, MERCK & CO, INC. makes no warranty with respect hereto and disclaims all liability from reliance thereon.

APPENDIX III

~~CONFIDENTIAL~~ FDA non-confidential per applicant

CERTIFICATION OF COMPLIANCE FROM MERCK

FOREIGN MANUFACTURER

Merck Sharp & Dohme (Ireland)
Ballydine, Kilsheelan
Clonmel,
Co. Tipperary,
Ireland.
Telephone (051) 640411
Fax (051) 640836

MERCK SHARP & DOHME

18 October 1996

Merck Sharp & Dohme (Ireland) states that it is in compliance with all local and national environmental laws, or on an enforceable schedule to be in compliance with all emission requirements set forth in all permits applicable to the production of Montelukast Sodium at its facility in Ballydine, Ireland and that any subsequent increase in production at the facility is not expected to affect compliance with the current emission requirements or compliance with environmental law.

D J. Buckley
Senior Director of Operations
Ballydine Plant, Merck Manufacturing Division.

18 Oct 1996

18 October 1996.

Patent Department

Merck & Co., Inc.
P.O. Box 2000
Rahway NJ 07065-0907
Fax 908 594 4720
Tel 908 594 4000
Cable MERCKRAH
Telex 138825

MERCK

January 28, 1997

Re: NDA 20-830 SINGULAIR™
(Montelukast Sodium Chewable Tablet)
Patent Information

Pursuant to the provisions of Section 505(b)(1) of the Federal Food, Drug and Cosmetic Act [21 USC 355(b)(1)] attached hereto please find the patent information for the above-identified application.

The undersigned declares that U.S. Patent No. 5,565,473 covers the compound, formulation, composition, and method of use of SINGULAIR™ (montelukast sodium chewable tablet), the subject of this application for which approval is being sought.

U.S. Patent No. 5,565,473 having an expiration date of November 30, 2010, claims the SINGULAIR™ active ingredient, montelukast sodium, as a compound, pharmaceutical compositions containing montelukast sodium, and the use of montelukast sodium in the treatment of asthma. US Patent No. 5,565,473 is owned by Merck Frosst Canada, Inc., a wholly owned subsidiary of Merck & Co., of Whitehouse Station, NJ.

A claim of patent infringement could be asserted if a person not licensed by the owner of U.S. Patent No. 5,565,473 engaged in the manufacture, use, offer to sell, sale, or importation into the United States of montelukast sodium.

Mollie M. Yang
(908) 594-6343

NDA 20-830 SINGULAIR™
(Montelukast Sodium Chewable Tablet)
Patent Information

Item 13

PATENT AND EXCLUSIVITY INFORMATION
MERCK RESEARCH LABORATORIES

1.	Active Ingredient:	Montelukast sodium
2.	Dosage:	5 mg
3.	Trade Name:	SINGULAIR™
4.	Dosage Forms:	Chewable Tablet
	Route of Administration:	Oral
5.	Applicant Firm Name:	Merck Research Laboratories
6.	NDA Number:	20-830
7.	Approval Date:	Pending
8.	Exclusivity - Date First ANDA Could be Submitted	Five years from the approval date of NDA 20-829
	Length of Exclusivity	To be determined
9.	Applicable Patent Numbers	5,565,473 Expiration Date: November 30, 2010

MERCK
Research Laboratories

Original NDA 20-830

Montelukast Sodium Chewable Tablets

Quality Assurance Statement

Merck Research Laboratories (MRL) data presented in this application were subject to audit by MRL Quality Assurance organizations based on approved standard operating procedures in effect at the time of the audit. A Quality Assurance statement and a statement of compliance are included with each nonclinical safety study report. For clinical research studies, an audit information page is provided for each clinical study report documenting external and internal auditing activities and an assessment of compliance to Good Clinical Practice standards for each protocol. Information presented in the label, synopsis and each summary section has been audited against the supporting documentation provided herein in accordance with Merck Research Laboratories Worldwide Quality Assurance Resources Standard Operating Procedures.

The quality assurance audits meet the following U.S. and international regulations and guidelines: U.S. Food and Drug Administration Code of Federal Regulations (21 CFR Part 58) and OECD Principles of Good Laboratory Practice (ISBN92-64-12367-9) and Rules Governing Medicinal products in the European Community Guidelines III/3700/90/EN.

EXCLUSIVITY SUMMARY for NDA # 20-830 SUPPL #_N/A____

Trade Name _Singulair Chewable Tablets_
Generic Name _montelukast sodium_

Applicant Name _Merck Research Laboratories___
HFD-_570___

Approval Date, if known _____

PART I IS AN EXCLUSIVITY DETERMINATION NEEDED?

1. An exclusivity determination will be made for all original applications, but only for certain supplements. Complete PARTS II and III of this Exclusivity Summary only if you answer "yes" to one or more of the following questions about the submission.

   a) Is it an original NDA?

   YES /_X_/ NO /___/

   b) Is it an effectiveness supplement?

   YES /___/ NO /_X_/

   If yes, what type? (SE1, SE2, etc.) _____

   c) Did it require the review of clinical data other than to support a safety claim or change in labeling related to safety? (If it required review only of bioavailability or bioequivalence data, answer "no.")

   YES /_X_/ NO /___/

   If your answer is "no" because you believe the study is a bioavailability study and, therefore, not eligible for exclusivity, EXPLAIN why it is a bioavailability study, including your reasons for disagreeing with any arguments made by the applicant that the study was not simply a bioavailability study.

   _____

   _____

   If it is a supplement requiring the review of clinical data but it is not an effectiveness supplement, describe the change or claim that is supported by the clinical data:

   _____

   _____

d) Did the applicant request exclusivity?

YES /_X_/ NO /___/

If the answer to (d) is "yes," how many years of exclusivity did the applicant request?

__5 years from date of approval_

IF YOU HAVE ANSWERED "NO" TO ALL OF THE ABOVE QUESTIONS, GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8.

2. Has a product with the same active ingredient(s), dosage form, strength, route of administration, and dosing schedule, previously been approved by FDA for the same use? (Rx-to-OTC switches should be answered NO-please indicate as such.)

YES /___/ NO /_X_/

If yes, NDA #_____ Drug Name _____

IF THE ANSWER TO QUESTION 2 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8.

3. Is this drug product or indication a DESI upgrade?

YES /___/ NO /_X_/

IF THE ANSWER TO QUESTION 3 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8 (even if a study was required for the upgrade).

PART II FIVE-YEAR EXCLUSIVITY FOR NEW CHEMICAL ENTITIES

(Answer either #1 or #2 as appropriate)

1. Single active ingredient product.

Has FDA previously approved under section 505 of the Act any drug product containing the same active moiety as the drug under consideration? Answer "yes" if the active moiety (including other esterified forms, salts, complexes, chelates or clathrates) has been previously approved, but this particular form of the active moiety, e.g., this particular ester or salt (including salts with hydrogen or coordination bonding) or other non-covalent derivative (such as a complex, chelate, or clathrate) has not been approved. Answer "no" if the compound requires metabolic conversion (other than deesterification of an esterified form of the drug) to produce an already approved active moiety.

YES /___/ NO /_X_/

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA# _____ _____

NDA# _____ _____

NDA# _____ _____

2. Combination product.

If the product contains more than one active moiety(as defined in Part II, #1), has FDA previously approved an application under section 505 containing any one of the active moieties in the drug product? If, for example, the combination contains one never-before-approved active moiety and one previously approved active moiety, answer "yes." (An active moiety that is marketed under an OTC monograph, but that was never approved under an NDA, is considered not previously approved.)

YES /___/ NO /_X_/

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA# _____ _____

NDA# _____ _____

NDA# _____ _____

IF THE ANSWER TO QUESTION 1 OR 2 UNDER PART II IS "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8. IF "YES" GO TO PART III.

PART III THREE-YEAR EXCLUSIVITY FOR NDA'S AND SUPPLEMENTS

To qualify for three years of exclusivity, an application or supplement must contain "reports of new clinical investigations (other than bioavailability studies) essential to the approval of the application and conducted or sponsored by the applicant." This section should be completed only if the answer to PART II, Question 1 or 2 was "yes."

1. Does the application contain reports of clinical investigations? (The Agency interprets "clinical investigations" to mean investigations conducted on humans other than bioavailability studies.) If the application contains clinical investigations only by virtue of a right of reference to clinical investigations in another application, answer "yes," then skip to question 3(a). If the answer to 3(a) is "yes" for any investigation referred to in another application, do not complete remainder of summary for that investigation.

YES /___/ NO /___/

IF "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8.

2. A clinical investigation is "essential to the approval" if the Agency could not have approved the application or supplement without relying on that investigation. Thus, the investigation is not essential to the approval if 1) no clinical investigation is necessary to support the supplement or application in light of previously approved applications (i.e., information other than clinical trials, such as bioavailability data, would be sufficient to provide a basis for approval as an ANDA or 505(b)(2) application because of what is already known about a previously approved product), or 2) there are published reports of studies (other than those conducted or sponsored by the applicant) or other publicly available data that independently would have been sufficient to support approval of the application, without reference to the clinical investigation submitted in the application.

(a) In light of previously approved applications, is a clinical investigation (either conducted by the applicant or available from some other source, including the published literature) necessary to support approval of the application or supplement?

YES /___/ NO /___/

If "no," state the basis for your conclusion that a clinical trial is not necessary for approval AND GO DIRECTLY TO SIGNATURE BLOCK ON PAGE 8:

_____

_____

YES /___/ NO /___/

(b) Did the applicant submit a list of published studies relevant to the safety and effectiveness of this drug product and a statement that the publicly available data would not independently support approval of the application?

YES /___/ NO /___/

(1) If the answer to 2(b) is "yes," do you personally know of any reason to disagree with the applicant's conclusion? If not applicable, answer NO.

YES /___/ NO /___/

If yes, explain: _____

_____

(2) If the answer to 2(b) is "no," are you aware of published studies not conducted or sponsored by the applicant or other publicly available data that could independently demonstrate the safety and effectiveness of this drug product?

YES /___/ NO /___/

If yes, explain: _____

_____

(c) If the answers to (b)(1) and (b)(2) were both "no," identify the clinical investigations submitted in the application that are essential to the approval:

_____

_____

Studies comparing two products with the same ingredient(s) are considered to be bioavailability studies for the purpose of this section.

3. In addition to being essential, investigations must be "new" to support exclusivity. The agency interprets "new clinical investigation" to mean an investigation that 1) has not been relied on by the agency to demonstrate the effectiveness of a previously approved drug for any indication and 2) does not duplicate the results of another investigation that was relied on by the agency to demonstrate the effectiveness of a previously approved drug product, i.e., does not redemonstrate something the agency considers to have been demonstrated in an already approved application.

a) For each investigation identified as "essential to the approval," has the investigation been relied on by the agency to demonstrate the effectiveness of a previously approved drug product? (If the investigation was relied on only to support the safety of a previously approved drug, answer "no.")

Investigation #1 YES /___/ NO /___/

Investigation #2 YES /___/ NO /___/

If you have answered "yes" for one or more investigations, identify each such investigation and the NDA in which each was relied upon:

_____ _____

_____ _____

b) For each investigation identified as "essential to the approval", does the investigation duplicate the results of another investigation that was relied on by the agency to support the effectiveness of a previously approved drug product?

Investigation #1 YES /___/ NO /___/

Investigation #2 YES /___/ NO /____/

If you have answered "yes" for one or more investigation, identify the NDA in which a similar investigation was relied on:

_____ _____

_____ _____

c) If the answers to 3(a) and 3(b) are no, identify each "new" investigation in the application or supplement that is essential to the approval (i.e., the investigations listed in #2(c), less any that are not "new"):

_____

_____ _____

4. To be eligible for exclusivity, a new investigation that is essential to approval must also have been conducted or sponsored by the applicant. An investigation was "conducted or sponsored by" the applicant if, before or during the conduct of the investigation, 1) the applicant was the sponsor of the IND named in the form FDA 1571 filed with the Agency, or 2) the applicant (or its predecessor in interest) provided substantial support for the study. Ordinarily, substantial support will mean providing 50 percent or more of the cost of the study.

a) For each investigation identified in response to question 3(c): if the investigation was carried out under an IND, was the applicant identified on the FDA 1571 as the sponsor?

Investigation #1

IND # YES /__/ NO /___/ Explain: _____

_____

Investigation #2

IND # YES /__/ NO /___/ Explain: _____

_____

(b) For each investigation not carried out under an IND or for which the applicant was not identified as the sponsor, did the applicant certify that it or the applicant's predecessor in interest provided substantial support for the study?

Investigation #1

YES /___/ Explain _____ NO /___/ Explain _____

_____ _____

_____ _____

Investigation #2

YES /___/ Explain _____ NO /___/ Explain _____

_____ _____

_____ _____

(c) Notwithstanding an answer of "yes" to (a) or (b), are there other reasons to believe that the applicant should not be credited with having "conducted or sponsored" the study? (Purchased studies may not be used as the basis for exclusivity. However, if all rights to the drug are purchased (not just studies on the drug), the applicant may be considered to have sponsored or conducted the studies sponsored or conducted by its predecessor in interest.)

YES /___/ NO /___/

If yes, explain: _____

_____

/S/

Signature

Title: Project Manager

23 January 1998

Date

/S/

Signature of Division Director

2/23/98

Date

cc: Original NDA Division File HFD-93 Mary Ann Holovac

DRUG STUDIES IN PEDIATRIC PATIENTS
(To be completed for all NME's recommended for approval)

NDA # 20 937 Trade (generic) names Singulair (montelukast sodium) Chewable Tablets

Check any of the following that apply and explain, as necessary, on the next page:

✓ 1. A proposed claim in the draft labeling is directed toward a specific pediatric illness. The application contains adequate and well-controlled studies in pediatric patients to support that claim.

___ 2. The draft labeling includes pediatric dosing information that is not based on adequate and well-controlled studies in children. The application contains a request under 21 CFR 210.58 or 314.126(c) for waiver of the requirement at 21 CFR 201.57(f) for A&MC studies in children.

___ a. The application contains data showing that the course of the disease and the effects of the drug are sufficiently similar in adults and children to permit extrapolation of the data from adults to children. The waiver request should be granted and a statement to that effect is included in the action letter.

___ b. The information included in the application does not adequately support the waiver request. The request should not be granted and a statement to that effect is included in the action letter. (Complete #3 or #4 below as appropriate.)

___ 3. Pediatric studies (e.g., dose-finding, pharmacokinetic, adverse reaction, adequate and well-controlled for safety and efficacy) should be done after approval. The drug product has some potential for use in children, but there is no reason to expect early widespread pediatric use (because, for example, alternative drugs are available or the condition is uncommon in children).

___ a. The applicant has committed to doing such studies as will be required.

___ (1) Studies are ongoing.
___ (2) Protocols have been submitted and approved.
___ (3) Protocols have been submitted and are under review.
___ (4) If no protocol has been submitted, on the next page explain the status of discussions.

___ b. If the sponsor is not willing to do pediatric studies, attach copies of FDA's written request that such studies be done and of the sponsor's written response to that request.

___ 4. Pediatric studies do not need to be encouraged because the drug product has little potential for use in children.

____ 5. If none of the above apply, explain.

Explain, as necessary, the foregoing items:

Singulair Tablets and Singulair Chewable Tablets are indicated for adult and pediatric patients 6 years of age and older for the prophylaxis and chronic treatment of asthma.

/S/

Signature of Preparer

7 February 1998

Date

cc: Orig NDA
HFD-___/Div File
NDA Action Package