

**CENTER FOR DRUG EVALUATION AND RESEARCH**

**APPROVAL PACKAGE FOR:**

**APPLICATION NUMBER**

**21-363**

**Administrative Documents**

## **DCL: Patent Information and Claim for Exclusivity**

### **Claim for Exclusivity (Section 20)**

1. Pursuant to the provisions of Sections 505(c)(3)(D)(iii) and 505 (j)(4)(D)(iii) of the Food, Drug and Cosmetic Act (FDCA) and 21 CFR 314.108 (b)(2), the applicant claims three (3) years of exclusivity for its Descarboethoxyloratadine tablets, for use in the treatment of the symptoms of seasonal and perennial allergic rhinitis in subjects 12 years of age and older.
2. The applicant certifies that to the best of the applicant's knowledge each of the clinical investigations included in the application meets the definition of "new clinical investigation" set forth in 21 CFR 314.108(a).
3. A list of all published studies or publicly available reports of clinical investigations known to the applicant through a computer-assisted literature search that are relevant to the conditions for which the applicant is seeking approval is provided as **Attachment 1**.
4. The applicant certifies that it has thoroughly searched the scientific literature through a computer-assisted search of the Scholar database, and Dialog database encompassing the subfiles MEDLINE, BIOSIS Previews, EMBASE and SciSearch, for English and non-English literature relating to tablets in humans, covering the period from to July, 1993 to March, 2001.
5. To the best of the applicant's knowledge, the list of scientific literature pertaining to descarboethoxyloratadine tablets is complete and accurate, and in the opinion of the applicant, such published studies or publicly available information do not provide a sufficient basis for the approval of the use of descarboethoxyloratadine tablets for the treatment of symptoms of seasonal and perennial allergic rhinitis without reference to the new information contained in the clinical trials in the application. The applicant's opinion that the studies or reports are insufficient is based on the following:
  - The literature does not contain adequate characterization of the efficacy and safety profile of descarboethoxyloratadine in the management of the



treatment of symptoms of seasonal and perennial allergic rhinitis, which is established by the data from the new clinical studies conducted by the applicant under IND [redacted] and included in this application.

6. The applicant was the sponsor named in the Form FDA-1571 for IND [redacted] under which the new clinical investigations were conducted.

APPEARS THIS WAY  
ON ORIGINAL



SCHOLAR

DES Loratadine AND ALLERGIC RHINITIS, DOCUMENTS ADDED ON OR AFTER 11/1/00  
2001/03/16

\*Doc ID: 00122004A

Drug Name/ Number: DESLORATADINE 034117  
Profile Drug Desloratadine

Anti-inflammatory properties of Desloratadine (DCL): Effect on eosinophil chemotaxis, adhesion and release of superoxide anions.

JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY  
(Jan., 2000) Vol. 105, No. 1 part 2, pp. S16-S17. Meeting Info.: 56th Annual Meeting of the American Academy of Allergy, Asthma and Immunology. San Diego, California, USA March 03-08, 2000 American Academy of Allergy, Asthma and Immunology .  
Agrawal DK  
Berro A  
KREUTNER W  
TOWNLEY RG

Study Type: in vitro

Abstract/Comment:

Desloratadine, which dose-dependently attenuated eosinophil chemotaxis, eosinophil adhesion to HUVECS, and superoxide generation, was possibly an effective anti-allergic drug.

\*Doc ID: 00122054A

Drug Name/ Number: DESLORATADINE 034117  
Profile Drug Desloratadine

Desloratadine improves quality of life in patients with seasonal allergic rhinitis.

JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY  
(Jan., 2000) Vol. 105, No. 1 part 2, pp. S383-S384. Meeting Info.: 56th Annual Meeting of the American Academy of Allergy, Asthma and Immunology. San Diego, California, USA March 03-08, 2000 American Academy of Allergy, Asthma and Immunology .  
Heithoff K  
MELTZER EO  
MELLARS L  
Salmun LM

Study Type: clinical

Abstract/Comment:

Seasonal allergic rhinitis patients who received desloratadine had improvements in their symptoms as well as improvements in their health-related quality of life.

\*Doc ID: 00123036A

Drug Name/ Number: DESLORATADINE 034117  
Profile Drug Desloratadine

Efficacy and safety of Desloratadine in seasonal allergic rhinitis.

JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY  
(Jan., 2000) Vol. 105, No. 1 part 2, pp. S384-S385. Meeting Info.: 56th  
Annual Meeting of the American Academy of Allergy, Asthma and  
Immunology. San Diego, California, USA March 03-08, 2000 American Academy  
of Allergy, Asthma and Immunology .

Salmun LM  
LORBER R  
DANZIG M  
STAUDINGER H

Study Type: clinical

Abstract/Comment:

In patients with seasonal allergic rhinitis, desloratadine at 5 or 7.5 mg/day for 14 days significantly improved total, nasal, and non-nasal symptom severity with few adverse effects.

\*Doc ID: 00193038A

Drug Name/ Number: DESLORATADINE 034117  
Profile Drug Desloratadine

(Summary of the American Academy of Asthma, Allergy and Immunology - 56th annual meeting. March meeting 3-8, 2000, San Diego, CA)

CURRENT OPINION IN ANTI-INFLAMMATORY IMMUNOMODULATORY INVESTIGATIONAL  
DRUGS

2,153-59, 2000

LIEBERMAN P

Study Type: clinical

experimental

Abstract/Comment:

Current research related to asthma, allergy, and immunology on desloratadine, albuterol, and mometasone was reviewed along with numerous other drugs. 0  
References

APPEARS THIS WAY  
ON ORIGINAL

**DATABASES SEARCHED:**

File 398:CHEMSEARCH(TM) 1957-2001/Feb  
(c) 2001 Amer.Chem.Soc.

SYSTEM:OS - DIALOG OneSearch

File 154:MEDLINE(R) 1993-2000/Dec W4  
(c) format only 2000 Dialog Corporation

\*File 154: Further to NLM notification, Medline updating is expected to resume in March 2001. For other NLM information see Help News154.

File 55:Biosis Previews(R) 1993-2001/Mar W2  
(c) 2001 BIOSIS

File 72:EMBASE 1993-2001/Mar W2  
(c) 2001 Elsevier Science B.V.

File 172:EMBASE Alert 2001/Mar W2  
(c) 2001 Elsevier Science B.V.

File 34:SciSearch(R) Cited Ref Sci 1990-2001/Mar W3  
(c) 2001 Inst for Sci Info

**APPEARS THIS WAY  
ON ORIGINAL**

**SEARCH STRATEGY:**

Set	Items	Description
S1	188	DESCARBOETHOXYLORATADINE + DESLORATADINE + SCH()34117 + RN- =100643-71-8
S2	56	"DESLORATADINE" OR R7-R12
S3	190	S1 OR S2
S4	3761	HAY(W)FEVER OR HAYFEVER
S5	22318	RHINITIS
S6	24368	S4 OR S5
S7	14	CLARINEX OR AERIUS
S8	203	S3 OR S7
S9	57	S6 AND S8
S10	52	S9/HUMAN
S11	41	S10/2000:2001
S12	26	RD (unique items)
S13	26	Sort S12/ALL/PY,D

APPEARS THIS WAY  
ON ORIGINAL

**DESLORATADINE AND ALLERGIC RHINITIS IN HUMANS  
DOCUMENTS PUBLISHED 2000-2001**

13/7/1 (Item 1 from file: 55)  
DIALOG(R)File 55:BIOSIS Previews(R)  
(c) 2001 BIOSIS. All rts. reserv.

12929508 BIOSIS NO.: 200100136657

Efficacy and tolerability of once-daily 5mg \*\*\*desloratadine\*\*\*, an H1-receptor antagonist, in patients with seasonal allergic \*\*\*rhinitis\*\*\* : Assessment during the spring and fall allergy seasons.

AUTHOR: Meltzer Eli O(a); Prenner Bruce M; Nayak Anjuli; Desloratadine Study Group

AUTHOR ADDRESS: (a)Allergy and Asthma Medical Group and Research Center, 9610 Granite Ridge Drive No. 13, San Diego, CA, 92123: eomeltzer@aol.com  
\*\*USA

JOURNAL: Clinical Drug Investigation 21 (1):p25-32 \*\*\*2001\*\*\*

MEDIUM: print

ISSN: 1173-2563

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

SUMMARY LANGUAGE: English

ABSTRACT: Objective: To evaluate the efficacy and tolerability of \*\*\*desloratadine\*\*\* 5mg once daily, a new, selective, H1-receptor antagonist, for the treatment of patients with seasonal allergic \*\*\*rhinitis\*\*\* (SAR) during the two major pollen seasons in the USA. Design: Two multicentre, randomised, double-blind, placebo-controlled, parallel-group investigations in patients with SAR are reported, one conducted during the spring (172 and 174 patients in the \*\*\*desloratadine\*\*\* and placebo groups, respectively) and the other during the fall (164 patients each in the \*\*\*desloratadine\*\*\* and placebo groups) allergy season. Study Participants: Patients 12 years of age or older with clinically symptomatic SAR and a minimum 2-year history of SAR. Interventions: \*\*\*Desloratadine\*\*\* 5mg or placebo once daily for 14 days following a 1-week screening period. Main Outcome Measures: The primary efficacy assessment was the mean change from baseline in the average reflective am/pm total symptom score (TSS) averaged over the 2-week study period. Results: In both seasons, \*\*\*desloratadine\*\*\* 5mg once daily resulted in a significant improvement in TSS for patients with SAR ( $p < 0.01$  and  $p = 0.02$ , respectively) over the 2-week study. Adverse events reported were mild to moderate in severity and similar to placebo. Assessment of sedation and ECG data revealed no clinically significant changes from baseline with \*\*\*desloratadine\*\*\*- or placebo-treated patients. Conclusion: \*\*\*Desloratadine\*\*\* 5mg once daily was effective and well tolerated in the treatment of symptoms associated with SAR following the first dose of therapy and continuing for the 2-week duration of the study during both the spring and fall allergy seasons.

13/7/2 (Item 2 from file: 72)

DIALOG(R)File 72:EMBASE

(c) 2001 Elsevier Science B.V. All rts. reserv.

11041831 EMBASE No: 2001074921

Approval for Schering-Plough drug

Manufacturing Chemist ( MANUF. CHEM. ) (United Kingdom) 2001, 72/2 (8)

CODEN: MCHMD ISSN: 0262-4230

DOCUMENT TYPE: Journal ; Note

LANGUAGE: ENGLISH

13/7/3 (Item 3 from file: 72)

DIALOG(R)File 72:EMBASE

(c) 2001 Elsevier Science B.V. All rts. reserv.

11037928 EMBASE No: 2001068916

\*\*\*Desloratadine\*\*\* activity in concurrent seasonal allergic

\*\*\*rhinitis\*\*\* and asthma

Baena-Cagnani C.E.

Dr. C.E. Baena-Cagnani, Santa Rosa 381, 5000 Cordoba Argentina

Allergy: European Journal of Allergy and Clinical Immunology, Supplement

( ALLERGY EUR. J. ALLERGY CLIN. IMMUNOL. SUPPL. ) (Denmark) 2001, 56/65  
(21-27)

CODEN: ALSUE ISSN: 0108-1675

DOCUMENT TYPE: Journal ; Review

LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

NUMBER OF REFERENCES: 43

Seasonal allergic \*\*\*rhinitis\*\*\* (SAR) and asthma, which are frequently comorbid, share some common allergic pathogenic bases. Clinical manifestations of these disorders might therefore be viewed as local manifestations of a systemic inflammatory state. Not only do the onsets of allergic-\*\*\*rhinitis\*\*\* (AR) and asthma symptoms often coincide (within 1 year), but also nasal challenges with SAR allergens can induce airways hyperreactivity (AHR). Eosinophils, which are key effector cells in both SAR and asthma, cause AHR, tissue damage, and neuronal effects through secretion of toxic granule proteins, enzymes, and other mediators. The novel, non-sedating, histamine H<sub>1</sub>-receptor antagonist, \*\*\*desloratadine\*\*\*, which exerts various favorable effects on the allergic cascade, significantly decreased SAR symptoms (e.g., nasal congestion) and diminished daily beta<sub>2</sub>-agonist use and improved asthma symptoms, while maintaining pulmonary function, in patients with SAR-asthma who were treated with oncedaily \*\*\*desloratadine\*\*\* regimens.

13/7/4 (Item 4 from file: 72)

DIALOG(R)File 72:EMBASE

(c) 2001 Elsevier Science B.V. All rts. reserv.

11037927 EMBASE No: 2001068915

Decongestant efficacy of \*\*\*desloratadine\*\*\* in patients with seasonal allergic \*\*\*rhinitis\*\*\*

Bachert C.

C. Bachert, ENT Department, University Hospital UZ Ghent, De Pintelaan  
185, B-9000 Ghent Belgium

Allergy: European Journal of Allergy and Clinical Immunology, Supplement

( ALLERGY EUR. J. ALLERGY CLIN. IMMUNOL. SUPPL. ) (Denmark) 2001, 56/65  
(14-20)

CODEN: ALSUE ISSN: 0108-1675

DOCUMENT TYPE: Journal ; Review

LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

NUMBER OF REFERENCES: 34

Recent advances in experimental immunologic approaches to seasonal allergic \*\*\*rhinitis\*\*\* (SAR) have led to a shift in the concepts of its pathogenesis. The conventional view of SAR as a local response to inhaled allergens has largely given way to a new view of this disorder as a systemic condition with local tissue manifestations. This concept, together with an increasing recognition of specific mediators' distinct roles in driving the early- and late-phase allergic responses, has opened multiple lines of therapeutic attack within the allergic cascade. Potent inhibition of inflammatory mediator release at distinct points in this cascade is conferred by \*\*\*desloratadine\*\*\*. In addition to the familiar range of SAR symptoms amenable to antihistamine therapy, \*\*\*desloratadine\*\*\* uniquely attenuates patient ratings of nasal congestion. This novel, non-sedating histamine H<sub>1</sub>-receptor antagonist is the only once-daily antiallergic product with a consistent decongestant effect that begins within hours of the first morning dose and is sustained for the entire treatment period.

13/7/5 (Item 5 from file: 72)

DIALOG(R)File 72:EMBASE

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11037926 EMBASE No: 2001068914

The pharmacologic profile of \*\*\*desloratadine\*\*\*: A review

Henz B.M.

Prof. B.M. Henz, Department of Dermatology, Humboldt University, Campus Virchow Klinikum, Augustenburgerplatz 1, 13344 Berlin Germany

Allergy: European Journal of Allergy and Clinical Immunology, Supplement ( ALLERGY EUR. J. ALLERGY CLIN. IMMUNOL. SUPPL. ) (Denmark) 2001, 56/65

(7-13)

CODEN: ALSUE ISSN: 0108-1675

DOCUMENT TYPE: Journal ; Review

LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

NUMBER OF REFERENCES: 45

\*\*\*Desloratadine\*\*\* is a new agent for the treatment of diseases such as seasonal allergic \*\*\*rhinitis\*\*\* and chronic urticaria. The pharmacologic profile of \*\*\*desloratadine\*\*\* offers particular benefits in terms of histamine H<sub>1</sub>-receptor binding potency and H<sub>1</sub> selectivity. \*\*\*Desloratadine\*\*\* has a half-life of 21-24 h, permitting once-daily dosing. No specific cautions are required with respect to administration in renal or hepatic failure, and food or grapefruit juice have no effect on the pharmacologic parameters. No clinically relevant racial or sex variations in the disposition of \*\*\*desloratadine\*\*\* have been noted. In combination with the cytochrome P450 inhibitors, ketoconazole and erythromycin, the AUC and C<sub>max</sub> of \*\*\*desloratadine\*\*\* were increased to a small extent, but no clinically relevant drug accumulation occurred. With high-dose treatment (45 mg/day for 10 days), no significant adverse events were observed, despite the sustained elevation of plasma \*\*\*desloratadine\*\*\* levels. Specifically, \*\*\*desloratadine\*\*\* had no effects on the corrected QT interval (QT<sub>c</sub>) when administered alone, at high

dose, or in combination with ketoconazole or erythromycin. Preclinical studies also show that \*\*\*desloratadine\*\*\* does not interfere with HERG channels or cardiac conduction parameters even at high dose.

\*\*\*Desloratadine\*\*\* is nonsedating and free of antimuscarinic/anticholinergic effects in preclinical and clinical studies. Novel anti-allergic and anti-inflammatory effects have also been noted with \*\*\*desloratadine\*\*\*, a fact which may be relevant to its clinical efficacy.

13/7/6 (Item 6 from file: 72)  
DIALOG(R)File 72:EMBASE  
(c) 2001 Elsevier Science B.V. All rts. reserv.

11037925 EMBASE No: 2001068913  
\*\*\*Desloratadine\*\*\*: A new approach in the treatment of allergy as a systemic disease - Pharmacology and clinical overview: Introduction  
Bonini S.  
S. Bonini, University of Naples, Institute of Neurobiology, Italian National Research Council, Rome Italy  
Allergy: European Journal of Allergy and Clinical Immunology, Supplement ( ALLERGY EUR. J. ALLERGY CLIN. IMMUNOL. SUPPL. ) (Denmark) 2001, 56/65 (5-6)  
CODEN: ALSUE ISSN: 0108-1675  
DOCUMENT TYPE: Journal ; Editorial  
LANGUAGE: ENGLISH

13/7/7 (Item 7 from file: 72)  
DIALOG(R)File 72:EMBASE  
(c) 2001 Elsevier Science B.V. All rts. reserv.

11013911 EMBASE No: 2001058980  
Efficacy and tolerability of once-daily 5mg \*\*\*desloratadine\*\*\*, an HSUB1-receptor antagonist, in patients with seasonal allergic \*\*\*rhinitis\*\*\*: Assessment during the spring and fall allergy seasons  
Meltzer E.O.; Prenner B.M.; Nayak A.  
Dr. E.O. Meltzer, Allergy/Asthma Med. Grp./Res. Ctr., 9610 Granite Ridge Drive, No. 13, San Diego, CA 92123 United States  
AUTHOR EMAIL: eomeltzer@aol.com  
Clinical Drug Investigation ( CLIN. DRUG INVEST. ) (New Zealand) 2001, 21/1 (25-32)  
CODEN: CDINF ISSN: 1173-2563  
DOCUMENT TYPE: Journal ; Article  
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH  
NUMBER OF REFERENCES: 16

Objective: To evaluate the efficacy and tolerability of \*\*\*desloratadine\*\*\* 5mg once daily, a new, selective, HSUB1-receptor antagonist, for the treatment of patients with seasonal allergic \*\*\*rhinitis\*\*\* (SAR) during the two major pollen seasons in the USA. Design: Two multicentre, randomised, double-blind, placebo-controlled, parallel-group investigations in patients with SAR are reported, one conducted during the spring (172 and 174 patients in the \*\*\*desloratadine\*\*\* and placebo groups, respectively) and the other during the fall (164 patients each in the \*\*\*desloratadine\*\*\* and placebo groups) allergy season. Study Participants: Patients 12 years of age or older with clinically symptomatic SAR and a minimum 2-year history of SAR.

Interventions: \*\*\*Desloratadine\*\*\* 5mg or placebo once daily for 14 days following a 1-week screening period. Main Outcome Measures: The primary efficacy assessment was the mean change from baseline in the average reflective am/pm total symptom score (TSS) averaged over the 2-week study period. Results: In both seasons, \*\*\*desloratadine\*\*\* 5mg once daily resulted in a significant improvement in TSS for patients with SAR ( $p < 0.01$  and  $p = 0.02$ , respectively) over the 2-week study. Adverse events reported were mild to moderate in severity and similar to placebo. Assessment of sedation and ECG data revealed no clinically significant changes from baseline with \*\*\*desloratadine\*\*\*- or placebo-treated patients. Conclusion: \*\*\*Desloratadine\*\*\* 5mg once daily was effective and well tolerated in the treatment of symptoms associated with SAR following the first dose of therapy and continuing for the 2-week duration of the study during both the spring and fall allergy seasons.

13/7/8 (Item 8 from file: 34)  
 DIALOG(R)File 34:SciSearch(R) Cited Ref Sci  
 (c) 2001 Inst for Sci Info. All rts. reserv.

09439847 Genuine Article#: 405RE Number of References: 0  
 Title: \*\*\*Desloratadine\*\*\* reduces the use of inhaled beta(2)-agonists and improves asthma symptoms in patients with seasonal allergic \*\*\*rhinitis\*\*\* and asthma  
 Author(s): Corren J  
 Corporate Author(s): Desloratadine Study Grp  
 Corporate Source: Allergy Res Fdn Inc, Los Angeles//CA/; Desloratadine Study Grp, Los Angeles//CA/  
 Journal: JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY, \*\*\*2001\*\*\*, V107, N2,S (FEB), PS163-S163  
 ISSN: 0091-6749 Publication date: 20010200  
 Publisher: MOSBY, INC, 11830 WESTLINE INDUSTRIAL DR, ST LOUIS, MO 63146-3318 USA  
 Language: English Document Type: MEETING ABSTRACT

13/7/9 (Item 9 from file: 34)  
 DIALOG(R)File 34:SciSearch(R) Cited Ref Sci  
 (c) 2001 Inst for Sci Info. All rts. reserv.

09439845 Genuine Article#: 405RE Number of References: 0  
 Title: \*\*\*Desloratadine\*\*\* reduces seasonal allergic \*\*\*rhinitis\*\*\* symptoms in patients with seasonal allergic \*\*\*rhinitis\*\*\* and asthma  
 Author(s): Berger WE  
 Corporate Author(s): Desloratadine Study Grp  
 Corporate Source: So Calif Res, Mission Viejo//CA/  
 Journal: JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY, \*\*\*2001\*\*\*, V107, N2,S (FEB), PS162-S162  
 ISSN: 0091-6749 Publication date: 20010200  
 Publisher: MOSBY, INC, 11830 WESTLINE INDUSTRIAL DR, ST LOUIS, MO 63146-3318 USA  
 Language: English Document Type: MEETING ABSTRACT

13/7/10 (Item 10 from file: 34)  
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci  
(c) 2001 Inst for Sci Info. All rts. reserv.

09439843 Genuine Article#: 405RE Number of References: 0  
Title: Long-term benefit of \*\*\*desloratadine\*\*\* against seasonal allergic  
\*\*\*rhinitis\*\*\* symptoms in patients with asthma  
Author(s): Ratner PH  
Corporate Author(s): Desloratadine Study Grp  
Corporate Source: Sylvania Res,San Antonio//TX/; Desloratadine Study Grp,San  
Antonio//TX/  
Journal: JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY, \*\*\*2001\*\*\*, V107, N2,S  
(FEB), PS161-S161  
ISSN: 0091-6749 Publication date: 20010200  
Publisher: MOSBY, INC, 11830 WESTLINE INDUSTRIAL DR, ST LOUIS, MO  
63146-3318 USA  
Language: English Document Type: MEETING ABSTRACT

13/7/11 (Item 11 from file: 34)  
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci  
(c) 2001 Inst for Sci Info. All rts. reserv.

09439842 Genuine Article#: 405RE Number of References: 0  
Title: Decongestant effects of \*\*\*desloratadine\*\*\* in patients with  
seasonal allergic \*\*\*rhinitis\*\*\* and asthma  
Author(s): Shapiro GG  
Corporate Author(s): Desloratadine Study Grp  
Corporate Source: Asthma Inc,Seattle//WA/; Desloratadine Study  
Grp,Seattle//WA/  
Journal: JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY, \*\*\*2001\*\*\*, V107, N2,S  
(FEB), PS161-S161  
ISSN: 0091-6749 Publication date: 20010200  
Publisher: MOSBY, INC, 11830 WESTLINE INDUSTRIAL DR, ST LOUIS, MO  
63146-3318 USA  
Language: English Document Type: MEETING ABSTRACT

13/7/12 (Item 12 from file: 34)  
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci  
(c) 2001 Inst for Sci Info. All rts. reserv.

09439839 Genuine Article#: 405RE Number of References: 0  
Title: Rapid onset of action of \*\*\*desloratadine\*\*\* in patients with  
seasonal allergic \*\*\*rhinitis\*\*\*  
Author(s): Meltzer EO  
Corporate Author(s): Desloratadine Study Grp  
Corporate Source: Allergy & Asthma Med Grp & Res Ctr,San Diego//CA/;  
Desloratadine Study Grp,San Diego//CA/  
Journal: JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY, \*\*\*2001\*\*\*, V107, N2,S  
(FEB), PS160-S160  
ISSN: 0091-6749 Publication date: 20010200  
Publisher: MOSBY, INC, 11830 WESTLINE INDUSTRIAL DR, ST LOUIS, MO  
63146-3318 USA  
Language: English Document Type: MEETING ABSTRACT

13/7/13 (Item 13 from file: 34)  
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci  
(c) 2001 Inst for Sci Info. All rts. reserv.

09439837 Genuine Article#: 405RE Number of References: 0  
Title: Once-daily \*\*\*desloratadine\*\*\* reduces the symptoms of perennial  
allergic \*\*\*rhinitis\*\*\* for at least 4 weeks  
Author(s): Dubuske LM  
Corporate Author(s): Desloratadine Study Grp  
Corporate Source: Immunol Res Inst New England, Boston//MA/; Desloratadine  
Study Grp, Boston//MA/  
Journal: JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY, \*\*\*2001\*\*\*, V107, N2, S  
(FEB), PS159-S159  
ISSN: 0091-6749 Publication date: 20010200  
Publisher: MOSBY, INC, 11830 WESTLINE INDUSTRIAL DR, ST LOUIS, MO  
63146-3318 USA  
Language: English Document Type: MEETING ABSTRACT

13/7/14 (Item 14 from file: 55)  
DIALOG(R)File 55:Biosis Previews(R)  
(c) 2001 BIOSIS. All rts. reserv.

12577374 BIOSIS NO.: 200000330876  
The pharmacokinetics, electrocardiographic effects, and tolerability of  
loratadine syrup in children aged 2 to 5 years.  
AUTHOR: Salmun Luis M(a); Herron Jerry M; Banfield Christopher; Padhi  
Desmond; Lorber Richard; Affrime Melton B  
AUTHOR ADDRESS: (a)Allergy/Respiratory Diseases Clinical Research,  
Schering-Plough Research Institute, 2000 Galloping Hill Road, Kenilworth,  
NJ, 07033-0539\*\*USA  
JOURNAL: Clinical Therapeutics 22 (5):p613-621 May, \*\*\*2000\*\*\*  
MEDIUM: print  
ISSN: 0149-2918  
DOCUMENT TYPE: Article  
RECORD TYPE: Abstract  
LANGUAGE: English  
SUMMARY LANGUAGE: English

ABSTRACT: Objective: We assessed the pharmacokinetics and tolerability of 5 mg loratadine syrup (1 mg/mL) in children aged 2 to 5 years. Methods: Two studies were undertaken. A single-dose, open-label bioavailability study was performed to characterize the pharmacokinetic profiles of loratadine and its metabolite \*\*\*desloratadine\*\*\*. Plasma concentrations of loratadine and \*\*\*desloratadine\*\*\* were determined at 0, 1, 2, 4, 8, 12, 24, 48, and 72 hours after a single administration of 5 mg loratadine syrup to 18 healthy children (11 male, 7 female; 12 black, 5 white, 1 other; mean age +- SD, 3.8 +- 1.1 years; mean weight +- SD, 17.4 +- 4.4 kg). In addition, a randomized, double-blind, placebo-controlled, parallel-group study was performed to assess the tolerability of 5 mg loratadine syrup after multiple doses. Loratadine (n = 60) or placebo (n = 61) was given once daily for 15 days to children with a history of allergic \*\*\*rhinitis\*\*\* or chronic idiopathic urticaria. In the loratadine group, 27 boys and 33 girls (52 white, 8 black) were enrolled, with a mean age +- SD of 3.67 +- 1.13 years and a mean weight +- SD of 17.2 +- 3.8 kg. In the placebo group, 27 boys and 34 girls (53 white, 7

black, 1 Asian) were enrolled, with a mean age  $\pm$  SD of 3.52  $\pm$  1.12 years and a mean weight  $\pm$  SD of 17.3  $\pm$  2.9 kg. Tolerability was assessed based on electrocardiographic results, occurrence of adverse events, changes in vital signs, and results of laboratory tests and physical examinations. Results: The peak plasma concentrations of loratadine and \*\*\*desloratadine\*\*\* were 7.78 and 5.09 ng/mL, respectively, observed 1.17 and 2.33 hours after administration of loratadine; the areas under the plasma concentration-time curve to the last quantifiable time point for loratadine and \*\*\*desloratadine\*\*\* were 16.7 and 87.2 ng $\cdot$ h/mL, respectively. Single and multiple doses were well tolerated, with no adverse events occurring with greater frequency after multiple doses of loratadine than after placebo. Electrocardiographic parameters were not altered by loratadine compared with placebo. There were no clinically meaningful changes in other tolerability assessments. Conclusion: Loratadine was well tolerated in this small, selected group of children aged 2 to 5 years at a dose providing exposure similar to that with the adult dose (ie, 10 mg once daily).

13/7/15 (Item 15 from file: 55)

DIALOG(R)File 55:Biosis Previews(R)

(c) 2001 BIOSIS. All rts. reserv.

12557078 BIOSIS NO.: 200000310580

\*\*\*Desloratadine\*\*\*: Treatment of allergic \*\*\*rhinitis\*\*\*, Histamine H1 antagonist.

AUTHOR: Graul A; Leeson P A; Castaner J

AUTHOR ADDRESS: (a)Prous Science, 08080, Barcelona\*\*Spain

JOURNAL: Drugs of the Future 25 (4):p339-346 April, \*\*\*2000\*\*\*

MEDIUM: print

ISSN: 0377-8282

DOCUMENT TYPE: Literature Review

RECORD TYPE: Citation

LANGUAGE: English

SUMMARY LANGUAGE: English

13/7/16 (Item 16 from file: 55)

DIALOG(R)File 55:Biosis Previews(R)

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12396305 BIOSIS NO.: 200000149807

Efficacy and safety of \*\*\*desloratadine\*\*\* in seasonal allergic \*\*\*rhinitis\*\*\*.

AUTHOR: Salmun L M(a); Lorber R(a); Danzig M(a); Staudinger H(a)

AUTHOR ADDRESS: (a)Schering-Plough Research Institute, Kenilworth, NJ\*\*USA

JOURNAL: Journal of Allergy and Clinical Immunology. 105 (1 part 2):p S384-S385 Jan., \*\*\*2000\*\*\*

CONFERENCE/MEETING: 56th Annual Meeting of the American Academy of Allergy, Asthma and Immunology. San Diego, California, USA March 03-08, 2000

SPONSOR: American Academy of Allergy, Asthma and Immunology

ISSN: 0091-6749

RECORD TYPE: Citation

LANGUAGE: English

SUMMARY LANGUAGE: English

13/7/17 (Item 17 from file: 55)  
 DIALOG(R)File 55:Biosis Previews(R)  
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12396304 BIOSIS NO.: 200000149806  
 Decongestant effects of \*\*\*desloratadine\*\*\* in patients with seasonal  
 allergic \*\*\*rhinitis\*\*\*.  
 AUTHOR: Nayak A(a); Lorber R; Salmun L M  
 AUTHOR ADDRESS: (a)Peoria School of Medicine, University of Illinois,  
 Peoria, IL\*\*USA  
 JOURNAL: Journal of Allergy and Clinical Immunology. 105 (1 part 2):pS384  
 Jan., \*\*\*2000\*\*\*  
 CONFERENCE/MEETING: 56th Annual Meeting of the American Academy of Allergy,  
 Asthma and Immunology. San Diego, California, USA March 03-08, 2000  
 SPONSOR: American Academy of Allergy, Asthma and Immunology  
 ISSN: 0091-6749  
 RECORD TYPE: Citation  
 LANGUAGE: English  
 SUMMARY LANGUAGE: English

13/7/18 (Item 18 from file: 55)  
 DIALOG(R)File 55:Biosis Previews(R)  
 (c) 2001 BIOSIS. All rts. reserv.

12396303 BIOSIS NO.: 200000149805  
 \*\*\*Desloratadine\*\*\* improves quality of life in patients with seasonal  
 allergic \*\*\*rhinitis\*\*\*.  
 AUTHOR: Heithoff K(a); Meltzer E O; Mellars L(a); Salmun L M(a)  
 AUTHOR ADDRESS: (a)Schering-Plough Research Institute, Kenilworth, NJ\*\*USA  
 JOURNAL: Journal of Allergy and Clinical Immunology. 105 (1 part 2):p  
 S383-S384 Jan., \*\*\*2000\*\*\*  
 CONFERENCE/MEETING: 56th Annual Meeting of the American Academy of Allergy,  
 Asthma and Immunology. San Diego, California, USA March 03-08, 2000  
 SPONSOR: American Academy of Allergy, Asthma and Immunology  
 ISSN: 0091-6749  
 RECORD TYPE: Citation  
 LANGUAGE: English  
 SUMMARY LANGUAGE: English

13/7/19 (Item 19 from file: 72)  
 DIALOG(R)File 72:EMBASE  
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10997115 EMBASE No: 2001042475  
 Present and potential therapy for allergic \*\*\*rhinitis\*\*\*: A review  
 Reichmuth D.; Lockey R.F.  
 Dr. D. Reichmuth, Division of Allergy and Immunology, Univ. of South FL  
 Coll. of Medicine, Tampa, FL United States  
 AUTHOR EMAIL: dreichmu@hsc.usf.edu  
 BioDrugs ( BIODRUGS ) (New Zealand) 2000, 14/6 (371-387)  
 CODEN: BIDRF ISSN: 1173-8804  
 DOCUMENT TYPE: Journal ; Review  
 LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH  
 NUMBER OF REFERENCES: 160

Allergic \*\*\*rhinitis\*\*\* can affect up to one-fifth of the population and the economic impact is increasing. HSUB1 receptor antagonists were the first major pharmacologic treatment, but the associated sedation limited their use. The 2 initial second generation less sedating antihistamines, astemizole and terfenadine, were found to prolong the cardiac QTSubc interval, especially when administered with other medications metabolised by the same cytochrome (CYP) P450 isoenzyme, CYP3A4. Other second generation antihistamines, fexofenadine, loratadine and cetirizine, do not cause clinically significant cardiac QTSubc interval prolongation. Two newer agents, ebastine and mizolastine, are also effective in the treatment of allergic \*\*\*rhinitis\*\*\*. Ebastine, however, prolongs the cardiac QTSubc interval in laboratory animals and humans, the clinical significance of which is unknown. \*\*\*Desloratadine\*\*\* and norastemizole, metabolites of loratadine and astemizole, respectively, are 2 other second generation antihistamines found to be effective treatments for seasonal allergic \*\*\*rhinitis\*\*\*. Unlike their parent compounds, they do not prolong the cardiac QTSubc interval. All clinically available intranasal corticosteroids are effective in the treatment of allergic \*\*\*rhinitis\*\*\*, but studies to evaluate possible long term systemic adverse effects are limited. Mometasone furoate and fluticasone propionate have lower oral bioavailability compared with other corticosteroids that are given intranasally. This may be important, since it is likely that some of the intranasal corticosteroid is ingested. Two 1-year growth studies in children indicated that intranasal beclomethasone dipropionate given twice daily reduces growth velocity, whereas intranasal mometasone furoate given once daily in the morning does not. Other studies are needed. Most but not all studies have shown that leukotriene antagonists are effective in the treatment of allergic \*\*\*rhinitis\*\*\*. HSUB1 receptor antagonists are not very effective in reducing nasal congestion, but leukotriene antagonists do attenuate this symptom. Furthermore, one study demonstrates an additive benefit in treating allergic \*\*\*rhinitis\*\*\* with the combination of a HSUB1 receptor and leukotriene antagonist. Clinical trials have demonstrated that anti-immunoglobulin (Ig) E is effective in the treatment of seasonal allergic \*\*\*rhinitis\*\*\* when free IgE is reduced to <25 mug/L. The reduction of total IgE is dose dependent and subcutaneous and intravenous administration are both effective. Immunotherapy is also an effective treatment for allergic \*\*\*rhinitis\*\*\*. CpG oligonucleotides is a novel adjuvant for allergen immunotherapy. This adjuvant used in a murine model shifts the immune response away from the allergic or TH2 phenotype. Studies in humans have not been performed.

13/7/20 (Item 20 from file: 72)

DIALOG(R)File 72:EMBASE

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10992705 EMBASE No: 2001034130

Use and safety of antihistamines in children

Chae K.M.; Tharp M.D.

Dr. M.D. Tharp, Department of Dermatology, RPSLMC, 630 S. Hermitage St.,  
Chicago, IL 60612 United States

Dermatologic Therapy ( DERMATOL. THER. ) (United States) 2000; 13/4  
(374-383)

CODEN: DETHF ISSN: 1396-0296

DOCUMENT TYPE: Journal ; Article

LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

NUMBER OF REFERENCES: 77

Although first-generation antihistamines remain popular for the treatment of seasonal allergic \*\*\*rhinitis\*\*\*, atopic dermatitis, and urticaria in children, second- and third-generation antihistamines hold clear advantages over the first-generation agents, especially for the pediatric patient. The less frequent dosing schedule of the second- and third-generation agents makes administration easier for the parent. With less sedation and lower risk of adverse effects, the safety profile of second- and third-generation agents appears superior to that of first-generation agents. After briefly discussing the use of first-generation antihistamines, the pharmacokinetics, safety, and use of the newer antihistamines loratadine, cetirizine, and fexofenadine in the pediatric patient are reviewed.

13/7/21 (Item 21 from file: 72)  
 DIALOG(R)File 72:EMBASE  
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10903859 EMBASE No: 2000387590  
 Norastemizole Sepracor  
 Bachmann K.A.  
 K.A. Bachmann, University of Toledo, College of Pharmacy, 2801 W Bancroft Street, Toledo, OH 43606 United States  
 AUTHOR EMAIL: kbachma@utnet.utoledo.edu  
 Current Opinion in Investigational Drugs ( CURR. OPIN. INVEST. DRUGS ) ( United Kingdom) 2000, 1/2 (219-226)  
 CODEN: CIDRE ISSN: 0967-8298  
 DOCUMENT TYPE: Journal; Review  
 LANGUAGE: ENGLISH  
 NUMBER OF REFERENCES: 112

13/7/22 (Item 22 from file: 72)  
 DIALOG(R)File 72:EMBASE  
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10737566 EMBASE No: 2000217587  
 Allergic \*\*\*rhinitis\*\*\*: Treating the adult  
 Corren J.  
 Dr. J. Corren, Allergy Research Foundation, Inc., 11620 Wilshire Blvd, Los Angeles, CA 90025 United States  
 Journal of Allergy and Clinical Immunology ( J. ALLERGY CLIN. IMMUNOL. ) (United States) 2000, 105/6 II (S610-S615)  
 CODEN: JACIB ISSN: 0091-6749  
 DOCUMENT TYPE: Journal; Conference Paper  
 LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH  
 NUMBER OF REFERENCES: 45

Allergic \*\*\*rhinitis\*\*\* is now recognized as a chronic medical condition that markedly affects patient quality of life and is a cause of substantial medical care expenditures. Effective treatment of adults with allergic \*\*\*rhinitis\*\*\* usually requires an integrated regimen that combines allergen avoidance measures, pharmacotherapy, and possible specific-allergen immunotherapy. This approach can control bothersome symptoms with minimal adverse effects in most patients. New medications, such as anti-immunoglobulin E therapy and cytokine antagonists, may provide relief to patients who are refractory to or do not tolerate currently available treatments.

13/7/23 (Item 23 from file: 72)  
DIALOG(R)File 72:EMBASE  
(c) 2001 Elsevier Science B.V. All rts. reserv.

10702681 EMBASE No: 2000190997  
\*\*\*Desloratadine\*\*\*. Treatment of allergic \*\*\*rhinitis\*\*\* histamine Hinf  
1 antagonist  
Graul A.; Leeson P.A.; Castaner J.  
A. Graul, Prous Science, P.O. Box 540, 08080 Barcelona Spain  
Drugs of the Future ( DRUGS FUTURE ) (Spain) 2000, 25/4 (339-346)  
CODEN: DRFUD ISSN: 0377-8282  
DOCUMENT TYPE: Journal; Article  
LANGUAGE: ENGLISH  
NUMBER OF REFERENCES: 45

13/7/24 (Item 24 from file: 72)  
DIALOG(R)File 72:EMBASE  
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10681480 EMBASE No: 2000164385  
American Academy of Asthma, Allergy and Immunology - 56th annual meeting:  
3-8 March 2000, San Diego, CA, USA  
Lieberman P.  
P. Lieberman, University of Tennessee, College of Medicine, Memphis, TN  
United States  
AUTHOR EMAIL: asthmamemphis@msn.com  
Current Opinion in Anti-inflammatory and Immunomodulatory Investigational  
Drugs ( CURR. OPIN. ANTI-INFLAMMATORY IMMUNOMODULATORY INVEST. DRUGS ) ( United Kingdom) 2000, 2/2 (153-159)  
CODEN: COAIF ISSN: 1464-8474  
DOCUMENT TYPE: Journal; Conference Paper  
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

San Diego, CA, recently hosted the 56th annual meeting of the American Academy of Asthma, Allergy and Immunology, held from March 3-8, 2000. The Academy is the largest allergy/asthma society in the US and perhaps the largest in the world. Its meeting reflected this size with over 6000 in attendance and with 1147 scientific presentations of cutting-edge research in the field of allergy and immunology. In addition, there were numerous workshops, seminars, and lectures. The activities oftentimes began as early as 6.30 am and ended as late as 9.00 pm. Superior powers seemed intent upon keeping participants indoors and learning by delivering the first hailstorm of recent memory in March in San Diego, a usually sunny haven of temperate weather.

13/7/25 (Item 25 from file: 72)  
DIALOG(R)File 72:EMBASE  
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10681476 EMBASE No: 2000164381  
\*\*\*Desloratadine\*\*\* Sepracor  
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Current Opinion in Anti-inflammatory and Immunomodulatory Investigational  
Drugs ( CURR. OPIN. ANTI-INFLAMMATORY IMMUNOMODULATORY INVEST. DRUGS ) ( United Kingdom) 2000, 2/2 (117-126)

CODEN: COAIF ISSN: 1464-8474

DOCUMENT TYPE: Journal; Review

LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

NUMBER OF REFERENCES: 90

The use of the loratadine metabolite, decarboethoxyloratadine (DCL), for the treatment of both allergic \*\*\*rhinitis\*\*\* and diabetic retinopathy is claimed. DCL is claimed to display fewer cardiovascular and tumor promoting side effects than loratadine. DCL was disclosed in US-04659716. DCL and loratadine were compared for antihistamine activity on guinea pig ileum. These gave IC<sub>50</sub> values of 0.98 and 18.6 nM, respectively. Inhibition of [<sup>3</sup>H]mepyramine binding to guinea pig cerebellar membranes was measured and IC<sub>50</sub> values of 51.1 and 721 nM were obtained. Mitogenic effects were assessed using a [<sup>3</sup>H]thymidine uptake assays in mouse splenocytes, and respective IC<sub>50</sub> values of 5.6 and 1.0 μM were obtained. The effects of DCL on the inwardly rectified potassium channel of cardiac monocytes were assessed. DCL is stated to be less active than terfenadine in this model. The synthesis of loratadine is described in US-04282233, and of DCL in US-04659716. The conversion of loratadine into DCL is described. Sample tablet and capsule formulations are provided. The only compound for which use is specifically claimed is decarboethoxyloratadine, 8-chloro-6,11-(4-piperidinylidene)-5H-benzo[5,6]cyclohepta[1,2b]pyridine.

13/7/26 (Item 26 from file: 72)

DIALOG(R)File 72:EMBASE

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10648088 EMBASE No: 2000113028

Fexofenadine: A review of its use in the management of seasonal allergic \*\*\*rhinitis\*\*\* and chronic idiopathic urticaria

Simpson K.; Jarvis B.

K. Simpson, Adis International Limited, 41 Centorian Drive, Mairangi Bay, Auckland 10 New Zealand

AUTHOR EMAIL: demail@adis.co.nz

Drugs ( DRUGS ) (New Zealand) 2000, 59/2 (301-321)

CODEN: DRUGA ISSN: 0012-6667

DOCUMENT TYPE: Journal; Review

LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

NUMBER OF REFERENCES: 78

Fexofenadine, the active metabolite of terfenadine, is a selective histamine H<sub>1</sub> receptor antagonist that does not cross the blood brain barrier and appears to display some anti-inflammatory properties. Fexofenadine is rapidly absorbed (onset of relief <=2 hours) and has a long duration of action, making it suitable for once daily administration. Clinical trials (<=2 weeks' duration) have shown fexofenadine 60mg twice daily and 120mg once daily to be as effective as loratadine 10mg once daily, and fexofenadine 120mg once daily to be as effective as cetirizine 10mg once daily in the overall reduction of symptoms of seasonal allergic \*\*\*rhinitis\*\*\*. When given in combination, fexofenadine and extended

release pseudoephedrine had complementary activity. Fexofenadine was effective in relieving the symptoms of sneezing, rhinorrhoea, itchy nose palate or throat, and itchy, watery, red eyes in patients with seasonal allergic \*\*\*rhinitis\*\*\*. There were often small improvements in nasal congestion that were further improved by pseudoephedrine. Fexofenadine produced greater improvements in quality of life than loratadine to an extent considered to be clinically meaningful, and enhanced patients' quality of life when added to pseudoephedrine treatment. Although no comparative data with other H<sub>1</sub> antagonists exist, fexofenadine 180mg once daily was effective in reducing the symptoms of chronic idiopathic urticaria for up to 6 weeks. Fexofenadine was well tolerated in clinical trials in adults and adolescents and the adverse event profile was similar to placebo in all studies. The most frequently reported adverse event during fexofenadine treatment was headache, which occurred with a similar incidence to that seen in placebo recipients. Fexofenadine does not inhibit cardiac K<sup>+</sup> channels and is not associated with prolongation of the corrected QT interval. When given alone or in combination with erythromycin or ketoconazole, it was not associated with any adverse cardiac events in clinical trials. As it does not cross the blood brain barrier, fexofenadine is free of the sedative effects associated with first generation antihistamines, even at dosages of up to 240 mg/day. Conclusions: fexofenadine is clinically effective in the treatment of seasonal allergic \*\*\*rhinitis\*\*\* and chronic idiopathic urticaria for which it is a suitable option for first-line therapy. Comparative data suggest that fexofenadine is as effective as loratadine or cetirizine in the treatment of seasonal allergic \*\*\*rhinitis\*\*\*. In those with excessive nasal congestion the combination of fexofenadine plus pseudoephedrine may be useful. In clinical trials fexofenadine is not associated with adverse cardiac or cognitive/psychomotor effects.

### **Debarment Certification**

Schering Corporation hereby certifies that it did not and will not use in any capacity the services of any person debarred under section 306 of the Federal Food, Drug and Cosmetic Act in connection with this application.



EXCLUSIVITY SUMMARY for NDA # 21-363 SUPPL # \_\_\_\_\_  
Trade Name Clarinox Generic Name desloratadine

Applicant Name Schering HFD- 570  
Approval Date February 8, 2002

**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 / \_\_\_/

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 /  / NO /  /

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

---

---

e) Has pediatric exclusivity been granted for this Active Moiety?

YES /  / NO /  /

**IF YOU HAVE ANSWERED "NO" TO ALL OF THE ABOVE QUESTIONS, GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9.**

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 /  /

If yes, NDA # \_\_\_\_\_ Drug Name \_\_\_\_\_

**IF THE ANSWER TO QUESTION 2 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9.**

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

YES /  / NO /  /

**IF THE ANSWER TO QUESTION 3 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9 (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 / X / NO / \_\_\_ /

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

NDA # 21-165 \_\_\_\_\_  
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 9. 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 / X / NO / \_\_\_ /

**IF "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9.**

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.

For the purposes of this section, studies comparing two products with the same ingredient(s) are considered to be bioavailability studies.

- (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 / X / 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 9:**

\_\_\_\_\_  
\_\_\_\_\_

- (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 / X / 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 / X /

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 / X /

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:

Investigation #1, Study # C00-218

Investigation #2, Study # C00-219

Investigation #3, Study # \_\_\_\_\_

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 / X /

Investigation #2 YES /\_\_\_/ NO / X /

Investigation #3 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:

NDA # \_\_\_\_\_ Study # \_\_\_\_\_  
 NDA # \_\_\_\_\_ Study # \_\_\_\_\_  
 NDA # \_\_\_\_\_ Study # \_\_\_\_\_

(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 / X /  
 Investigation #2                      YES /\_\_\_/                      NO / X /  
 Investigation #3                      YES /\_\_\_/                      NO /\_\_\_/

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

NDA # \_\_\_\_\_ Study # \_\_\_\_\_  
 NDA # \_\_\_\_\_ Study # \_\_\_\_\_  
 NDA # \_\_\_\_\_ Study # \_\_\_\_\_

(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"):

Investigation # 1, Study # C00-218  
 Investigation # 2, Study # C00-219  
 Investigation #   , Study # \_\_\_\_\_

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.





**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 / X / NO / \_\_\_ /

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

NDA # 21-165 \_\_\_\_\_

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 / X / NO / \_\_\_ /

**PEDIATRIC PAGE**

(Complete for all original applications and all efficacy supplements)

NOTE: A new Pediatric Page must be completed at the time of each action even though one was prepared at the time of the last action.

NDA/BLA # 21-363 Supplement # \_\_\_\_\_ Circle one: SE1 SE2 SE3 SE4 SE5 SE6

HFD-570 Trade and generic names/dosage form: Clarinet (desloratidine) Action: AP AE NA

Applicant Schering Corporation Therapeutic Class 601

Indication(s) previously approved Seasonal Allergic Rhinitis

Pediatric information in labeling of approved indication(s) is adequate \_\_\_ inadequate X

Proposed indication in this application Perennial Allergic Rhinitis

FOR SUPPLEMENTS, ANSWER THE FOLLOWING QUESTIONS IN RELATION TO THE PROPOSED INDICATION. IS THE DRUG NEEDED IN ANY PEDIATRIC AGE GROUPS? \_\_\_ Yes (Continue with questions) \_\_\_ No (Sign and return the form)

WHAT PEDIATRIC AGE GROUPS IS THE DRUG NEEDED? (Check all that apply)

\_\_\_ Neonates (Birth-1month) X Infants (6month-2yrs) X Children (2-12yrs) \_\_\_ Adolescents(12-16yrs)

\_\_\_ 1. PEDIATRIC LABELING IS ADEQUATE FOR ALL PEDIATRIC AGE GROUPS. Appropriate information has been submitted in this or previous applications and has been adequately summarized in the labeling to permit satisfactory labeling for all pediatric age groups. Further information is not required.

\_\_\_ 2. PEDIATRIC LABELING IS ADEQUATE FOR CERTAIN AGE GROUPS. Appropriate information has been submitted in this or previous applications and has been adequately summarized in the labeling to permit satisfactory labeling for certain pediatric age groups (e.g., infants, children, and adolescents but not neonates). Further information is not required.

X 3. PEDIATRIC STUDIES ARE NEEDED. There is potential for use in children, and further information is required to permit adequate labeling for this use.

X a. A new dosing formulation is needed, and applicant has agreed to provide the appropriate formulation.

\_\_\_ b. A new dosing formulation is needed, however the sponsor is either not willing to provide it or is in negotiations with FDA.

\_\_\_ c. The applicant has committed to doing such studies as will be required.  
\_\_\_ (1) Studies are ongoing,  
\_\_\_ (2) Protocols were submitted and approved.  
\_\_\_ (3) Protocols were submitted and are under review.  
\_\_\_ (4) If no protocol has been submitted, attach memo describing status of discussions.

\_\_\_ d. 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 ARE NOT NEEDED. The drug/biologic product has little potential for use in pediatric patients. Attach memo explaining why pediatric studies are not needed.

5. If none of the above apply, attach an explanation, as necessary.