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

[Logo: SCHERING-PLOUGH RESEARCH INSTITUTE]
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 and included in this application.

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

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.
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.
Salmon 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.
(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
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
(c) 2001 Elsevier Science B.V.
File 172: EMBASE Alert 2001/Mar W2
(c) 2001 Elsevier Science B.V.
(c) 2001 Inst for Sci Info
**SEARCH STRATEGY:**

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DESLOTRADINE 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
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.
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

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, nonsedating, histamine H1-sub1-receptor antagonist,
***desloratadine***, which exerts various favorable effects on the allergic
cascade, significantly decreased SAR symptoms (e.g., nasal congestion) and
diminished daily beta2-agonist use and improved asthma symptoms, while
maintaining pulmonary function, in patients with SAR-asthma who were
treated with oncedaily ***desloratadine*** regimens.

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
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 H1-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)
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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 H1-receptor binding potency and H1 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 Cmax 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 levels. Specifically, desloratadine had no effects on the corrected QT interval (QTc) 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 non-sedating and free of antimuscarinic/anticholinergic effects in preclinical and clinical studies. Novel antiallergic and anti-inflammatory effects have also been noted with desloratadine, a factor 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 H1-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, 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.
13/7/10  (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: Sylvana 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
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
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

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; Affrine 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 +/- SD of 3.52 +/- 1.12
years and a mean weight +/- SD of 17.3 +/- 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 ngcntdtos/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
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)
(c) 2001 BIOSIS. All rts. reserv.
12396305   BIOSIS NO.: 200000149807
Efficacy and safety of ***desloratadine*** in seasonal allergic
***rhinitis***.
AUTHOR: Salum M 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
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

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

**AUTHOR**: Heitloff 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): pS383-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

---

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@hs.c.usf.edu

BioDrugs ( BIODRUGS ) (New Zealand) 2000, 14/6 (371-387)

**CODEN**: BIDRFB  **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 QT SUBC 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 QT SUBC interval prolongation. Two newer agents, ebastine and mizolastine, are also effective in the treatment of allergic ***rhinitis***. Ebastine, however, prolongs the cardiac QT SUBC 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 QT SUBC 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 mg/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.
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@utneut.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
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10702681 EMBASE No: 2000190997
***Desloratadine***. Treatment of allergic ***rhinitis*** histamine H1 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: DRFUDI 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: asthmanmemphis@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
Norman P.
P. Norman, Norman Consulting, 18 Pink Lane, Burnham, Bucks SL1 8JW
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\(_{50}\) 5inf 0 values of 0.98 and 18.6 nM, respectively. Inhibition of [sup 3H]mepyramine binding to guinea pig cerebellar membranes was measured and IC\(_{50}\) 5inf 0 values of 51.1 and 721 nM were obtained. Mitogenic effects were assessed using a [sup 3H]thymidine uptake assays in mouse splenocytes, and respective IC\(_{50}\) 5inf 0 values of 5.6 and 1.0 \(\mu\)M 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-piperadinyllidine)-5H-benzo[5,6]cyclohepta[1,2b]pyridine.

Fexofenadine, the active metabolite of terfenadine, is a selective histamine H\(_1\) 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, rhinorrhea, 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 H1 antihistaminics 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+ 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 pseudephedrine 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 # HFD- 570
Trade Name Clarinex Generic Name desloratadine
Applicant Name Schering 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(SEL, 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?

________________________________________

________________________________________

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

YES / ___ / NO / X /

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 / X /

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 / X / 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 # ________________

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:
(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?

<table>
<thead>
<tr>
<th>Investigation #</th>
<th>YES /___/</th>
<th>NO /x/</th>
</tr>
</thead>
<tbody>
<tr>
<td>Investigation #1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Investigation #2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Investigation #3</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>NDA #</th>
<th>Study #</th>
</tr>
</thead>
<tbody>
<tr>
<td>NDA #</td>
<td>Study #</td>
</tr>
<tr>
<td>NDA #</td>
<td>Study #</td>
</tr>
</tbody>
</table>

(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"):

<table>
<thead>
<tr>
<th>Investigation #</th>
<th>Study #</th>
</tr>
</thead>
<tbody>
<tr>
<td>Investigation #1</td>
<td>COO-218</td>
</tr>
<tr>
<td>Investigation #2</td>
<td>COO-219</td>
</tr>
</tbody>
</table>

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 / X / NO / ___ / Explain: ______

Investigation #2
IND # ___________ YES / X / 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: __________________________________________

________________________________________________________

Signature of Preparer  2/7/02
Title: Regulatory Management Officer

Date

Signature of Office or Division Director

Date

CC:
Archival NDA
HFD- __/Division File
HFD- __/RPM
HFD-093/Mary Ann Holovac
HFD-104/PEDS/T.Crescenzi

Form OGD-011347
Revised 8/7/95; edited 8/8/95; revised 8/25/98, edited 3/6/00

Page 9
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 end 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: Clarinex (desloratidine)  Action: AP  AE  NA

Applicant: Schering Corporation  Therapeutic Class: ☐

Indication(s) previously approved: ☐ Seasonal Allergic Rhinitis

Pediatric information in labeling of approved indication(s) is adequate: ☑ inadequate: ☒

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-1 month)  ☑ Infants (6 month-2 yrs)  ☒ Children (2-12 yrs)  ☐ Adolescents (12-16 yrs)

☐ 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.

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

☒ 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.