

# **One Year Post Exclusivity Adverse Event Review: Desloratadine**

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# Background Drug Information

- **Moiety:** Clarinex<sup>®</sup> (desloratadine) Tablets, Syrup, Reditabs<sup>®</sup> Tablets
- **Therapeutic Category:** Anti-histamine
- **Sponsor:** Schering Corporation
- **Original Market Approval:** December 21, 2001
- **Pediatric Exclusivity Granted:** February 12, 2003

# Background Drug Information

- **Indications:**

- Seasonal allergic rhinitis in patients > 2 years old
- Perennial allergic rhinitis and chronic idiopathic urticaria in patients > 6 months of age

- **Dosages:**

- Adults and children > 12 y.o.: 5 mg once daily
- Children 6 to 11 y.o.: 2.5 mg once daily
- Children 1 to 5 y.o.: 1.25 mg once daily
- Children 6 to 11 months : 1 mg once daily

# Loratadine vs. Desloratadine

- Loratadine is approved for children  $>2$  y.o. and desloratadine is approved for children  $> 6$  months of age.
- Desloratadine is the major metabolite of loratadine and possesses similar pharmacodynamic activity.
- Desloratadine has less extensive first-pass metabolism and a longer half-life than loratadine.

# Drug Use Trends in Outpatient Settings: Desloratadine

- Desloratadine accounted for approximately 15% of the prescription non-sedating, anti-histamine market during March 2003 to February 2004.<sup>1</sup>
- The total number of desloratadine products prescribed increased from 9.8 million during March 2002 to February 2003 to 10.2 million during March 2003 to February 2004.<sup>1</sup>
- Pediatric patients accounted for approximately 13% of total U.S. prescriptions of desloratadine in 2003 (1.3 million).<sup>1,2\*</sup>
  - 1-<12 yrs = 604,000 prescriptions (5.9 %)
  - 12-16 yrs = 727,000 prescriptions (7.1 %)

<sup>1</sup>IMS Health, National Prescription Audit *Plus?* , On-Line Source, Mar 2001 – Feb 2004, Data Extracted Apr 2004

<sup>2</sup>AdvancePCS? Dimension Rx, On-Line, Mar 2002 –Feb 2004

\*Calculation based on application of proportions of pediatric desloratadine prescriptions in AdvancePCS? to IMS Health, National Prescription Audit *Plus?* to estimate number of desloratadine prescriptions dispensed nationwide to pediatric population

# Clinical Studies for Exclusivity

- 246 children, 6 months to 11 years of age, with a documented history of allergic rhinitis, chronic idiopathic urticaria, or patients who were candidates for anti-histamine.
- Three 15-day, double-blind, placebo-controlled safety studies were performed.
  - 60 children, 6-11 y.o. received 2.5 mg of desloratadine
  - 55 children, 2-5 y.o. received 1.25 mg of desloratadine
  - 65 children 12 to 23 months received 1.25 mg and 66 children 6 to 11 months received 1mg of desloratadine

# Clinical Studies for Exclusivity

- Efficacy extrapolated from well controlled studies performed in the adult population
- Safety studies identified a subset of pediatric patients (approx. 6% of all pediatric and adult subjects and 17% of the African-American subjects studied) who are slow metabolizers of desloratadine (half-life exceeding 50 hours)
- No difference in the prevalence of poor metabolizers across age groups
- There is no significant difference in adverse events, laboratory tests, or vital signs between pediatric poor metabolizers who receive desloratadine and pediatric normal metabolizers who receive desloratadine or placebo

# Adverse Events From Clinical Trials Included in the Label

- The following adverse events occurred >2% during the clinical trials, in adults and children > 12 years of age:
  - headache, nausea, fatigue, pharyngitis, dizziness, dyspepsia, myalgia, dry mouth, somnolence, dysmenorrhea.

# Adverse Events From Clinical Trials Included in the Label

- No adverse events reported by 2% of the patients in the 6 to 11 y.o. group.
- A.E. = 2% and frequency greater than placebo:
  - 2 to 5 y.o.: fever, urinary tract infection and varicella
  - 12 to 23 months: fever, diarrhea, upper respiratory tract infections, coughing, appetite increased, emotional lability, epistaxis, parasitic infection, pharyngitis, maculopapular rash.
  - 6 to 11 months: upper respiratory tract infections, diarrhea, fever, irritability, coughing, somnolence, bronchitis, otitis media, vomiting, anorexia, pharyngitis, insomnia, rhinorrhea, erythema, nausea.

# Adverse Event Reports :

## Desloratadine

### February 2003 – March 2004

- Total number of reports, all ages:
  - 185 reports (88 US)
- Pediatric reports:
  - 20 unduplicated reports (6 US)
    - 5 serious pediatric adverse events:
      - 4 hospitalizations
      - 3 life threatening events (includes two of the hospitalizations)
  - No deaths

# Pediatric Adverse Event Reports

## Desloratadine (n=20)

### February 2003 – March 2004

- Congenital anomalies (2)
- Somnolence (2)
- Movement disorders (4)
- Hypersensitivity reactions (4)
- Asthma (2)
- Abdominal pain (2)
- Bronchitis (1)
- Drug ineffective (1)
- Frequent urination (1)
- Benign Intracranial hypertension (1)
- Bradycardia and syncope (1)
- Kawasaki's Disease (1)

Underlined= unlabeled events

## 5 Serious Adverse Event Reports

- 12 y.o. on desloratadine, 5 mg and nasal beclomethasone for unspecified allergy, had bronchospasm, and shortness of breath; hospitalized for unknown period of time (Non-US)
- 11 y.o. on desloratadine, 5 mg daily, unknown indication, developed 2 asthma attacks within 1 month requiring hospitalization; the patient had five doses of the drug between the asthma attacks without difficulty (Non-US)
- 6 y.o. on desloratadine, 2.5 mg daily for urticaria, presented with Kawasaki Disease 3 months later (Non-US)

# 5 Serious Adverse Event Reports (cont.)

- 5 y.o. on desloratadine, 1.25 mg daily for cough and nasal secretion, experienced somnolence, bradycardia, diplopia, dizziness, and motor incoordination; hospitalized for 12 hours (Non-US)
- 2 y.o. with a history of bronchiolitis and wheezing, on desloratadine 1.25 mg for coughing and rhinitis, experienced status asthmaticus requiring hospitalization on 2 successive days (Non-US)

# Other Relevant Adverse Events

- 5 y.o. on desloratadine, 1.25 mg daily for rhinitis, experienced two days later somnolence, disorientation, an unspecified extrapyramidal disorder; one week later became unconscious; recovered one day after the drug was discontinued (Non-US)
- 4 y.o. girl on desloratadine, 2.5 mg daily for 1 week for mosquito bites, no other medications; experienced spasms of the upper body; resolved weeks later after discontinuation of the drug (Non-US)

## Other Relevant Adverse Events

- 3 y.o. on desloratadine for 8 days, unknown dose, unspecified indication, no concomitant medications experienced torticollis; no other data available (Non-US)

# Summary

- There were few pediatric adverse event reports during the Pediatric Exclusivity Period
- There are no new safety concerns regarding the use of desloratadine in the pediatric population
- This completes the one-year post-exclusivity adverse event monitoring as mandated by BPCA.
- FDA will continue its routine monitoring of adverse events for this drug.