PRESCRIBING INFORMATION

APO-LORATADINE
Loratadine Tablets
10 mg

THERAPEUTIC CLASSIFICATION

Histamine H_1 Receptor Antagonist

ACTIONS AND CLINICAL PHARMACOLOGY

Loratadine is a long-acting tricyclic antihistamine with selective peripheral H_1 receptor antagonistic activity. It exhibits a dose-related inhibition of the histamine-induced skin wheal and flare response in humans which is rapid in onset, is apparent at two hours and persists throughout the 24 hour observation period. Single oral doses up to 160 mg and repeat daily doses of 40 mg for up to 13 weeks were well tolerated with the incidence of sedation and dry mouth being no different from placebo.

^{14}C-loratadine is rapidly absorbed reaching C_{max} values (4.7, 10.8 and 26.1 ng/mL) at 1.5, 1.0 and 1.3 hours for the 10, 20 and 40 mg dose, respectively. The loratadine elimination half-life ($t_{1/2\beta}$) ranged from 7.8 - 11.0 hours. Descarboethoxyloratadine, the major active metabolite, reached C_{max} values (4.0, 9.9 and 16.0 ng/mL) at 3.7,1.5 and 2.0 hours after a dose of 10, 20 and 40 mg, respectively. Its $t_{1/2\beta}$ ranged from 17 to 24 hours. The accumulation indices, calculated by C_{max} and the area under the curve (AUC) ratios did not change after the 5th day, indicating little or no accumulation of either loratadine or its metabolite after a multiple once per day dosage regimen. The $t_{1/2\beta}$ at steady state levels for loratadine and its metabolite were 14.4 and 18.7 hours, respectively, similar to that reported following a single oral dose.

Approximately 82% of the ^{14}C-loratadine dose is excreted in the urine (40%) and feces (42%) over a 10-day period. Approximately 27% of the dose is eliminated in the urine during the first 24 hours largely in the conjugated form. Unchanged drug is present only in trace quantities in the urine and the active metabolite descarboethoxyloratadine represents only 0.4 to 0.6% of the administered loratadine dose.

INDICATIONS AND CLINICAL USE

APO-LORATADINE (loratadine) is indicated for the relief of symptoms associated with seasonal and perennial allergic rhinitis, such as sneezing, nasal discharge and itching, and ocular itching and burning, and for the relief of symptoms and signs of chronic urticaria and other allergic dermatologic disorders. Clinical studies to date support treatment for up to 6 months, thus medical recommendation is advised for longer-term use.

CONTRAINDICATIONS

APO-LORATADINE (loratadine) is contraindicated in patients who have shown hypersensitivity or idiosyncrasy to the drug or its components.

PRECAUTIONS

Use in Pregnancy and in Nursing Mothers
The safe use of loratadine during pregnancy or lactation has not been established and therefore the compound should be used only if the potential benefit justifies the potential risk to fetus or infant.

Use in Children
The safety and efficacy of loratadine in children younger than 2 years of age have not been established. Long term safety and efficacy of loratadine in children between the ages of 2 and 12 have not been demonstrated. Therefore, it is desirable that APO-LORATADINE (loratadine) not be administered to children between the ages of 2 and 12 for longer than 14 days, unless recommended by a physician.

Use in Patients with Liver impairment
Patients with severe liver impairment should be administered a lower initial dose because they may have reduced clearance of loratadine; an initial dose of 5 mg once daily or 10 mg every other day is recommended.

ADVERSE REACTIONS

Adverse experiences reported with loratadine in adults during the clinical trials were mild and consisted of fatigue, headache, dry mouth and sedation. The incidence of sedation was similar to that of the comparative agents terfenadine, astemizole and placebo, but statistically different ($p<0.01$) from clemastine (see table 1). In addition to those listed in table 1, the following were reported less frequently (less than 1 %): appetite increased, coughing, dizziness, nausea and palpitations.

Adverse experiences reported in pediatric patients are shown in Table 2. Nervousness and hyperkinesia were among the reported adverse experiences. One case of hyperkinesia was graded as severe and was judged by the physician to be possibly related to loratadine treatment. Gastrointestinal adverse reactions reported during pediatric trials may have been slightly more frequent in the younger patients (less than or equal to 30 kg), but in older children (greater than 30 kg) is similar to placebo (Table 3).

During the marketing of loratadine, alopecia, anaphylaxis and abnormal hepatic function have been reported rarely.

Drug Interactions:
When administered concomitantly with alcohol, loratadine has no potentiating effects as measured by psychomotor performance studies.

Increases in plasma concentrations of loratadine have been reported after concomitant use with ketoconazole, erythromycin or cimetidine in controlled clinical trials, but without clinically significant changes (including electrocardiographic). Other drugs known to inhibit hepatic metabolism should be coadministered with caution until definitive interaction studies can be completed.

Drug/Laboratory Test Interactions : Loratadine should be discontinued approximately 48 hours prior to skin testing procedures since antihistamines may prevent or diminish otherwise positive reactions to dermal reactivity indicators.

TABLE 1: ADVERSE EXPERIENCES REPORTED IN ADULT PATIENTS

Loratadine Tablets, 10 mg Once Daily vs Placebo and Comparatives

Number (%) of Adult Patients Reporting Frequently Occurring (>2% of loratadine-treated patients) Adverse Experiences in Adults Possibly or Probably Related to Treatment: Patients Treated with Loratadine, Placebo and Comparative

Adverse Experience	Loratadine 10 mg OD N =1241	Placebo N = 1652	Clemastine 1 mg BID N = 687	Terfenadine 60 mg BID N = 506	Astemizole 10 mg OD N = 342
Fatigue	54 (4)	62 (4)	62 (9)	17 (3)	22 (6)
Headache	97 (8)	104 (6)	32 (5)	40 (8)	26 (7)
Dry Mouth	49 (4)	32 (2)	22 (5)	15 (3)	2 (1)
Dryness in nose	9 (>1)	-	6 (>1)	3 (>1)	-
Sedation*	99 (8)	101 (6)	151 (22)	41 (8)	50 (15)

* Reported as somnolence, sleepiness, drowsiness, lethargy, slow or "drugged feeling"

TABLE 2: ADVERSE EXPERIENCES REPORTED IN PEDIATRIC PATIENTS

Loratadine Syrup, 1 mg/mL, 5-10 mg Once Daily

Number (%) of Pediatric Patients Reporting Frequently Occurring (≥2% of loratadine-treated patients) Treatment-Related Adverse Experiences: Placebo-Controlled Clinical Trials in Pediatric Studies in Seasonal Allergic Rhinitis and Allergic Skin Disorder Studies

Adverse Experience	Loratadine 5 mg N = 46	Loratadine 10 mg N = 119	Chlorpheniramine 2 mg N = 48	Chlorpheniramine 4 mg N = 112	Placebo N = 168
Nervousness	2 (4)	5 (4)	1 (2)	2 (2)	2 (1)
Hyperkinesia	0 (0)	4 (3)	0 (0)	1 (1)	1 (0.6)
Sedation	2 (4)	6 (5)	4 (8)	13 (11)	9 (5)
Headache	3 (6)	4 (3)	4 (8)	5 (4)	13 (8)

TABLE 3

Number (%) of Pediatric Patients Reporting Gastrointestinal Adverse Experience in Placebo-Controlled Clinical Trials Possibly or Probably Related to Study Medication, Grouped According to Treatment, Dose, Weight, in Pediatric Studies

Adverse Event	5 mg Dose Wt ≤ 30 kg (N =46)	10 mg Dose Wt > 30 kg (N = 119)	Placebo Wt > 30 kg (N = 168)
Diarrhea	1	0	0
Nausea	2	2	5
Dyspepsia	2	3	3
Vomiting	2	0	0
Abnormal Pain	0	2	0
Total	7 (15%)	8 (6.8%)	8 (4.8%)

SYMPTOMS AND TREATMENT OF OVERDOSAGE

Somnolence, tachycardia and headache have been reported with overdoses of the conventional loratadine formulation. A single acute ingestion of 160 mg produced no adverse effects.

In the event of overdosage, treatment, which should be started immediately, is symptomatic and supportive. Discontinuation of use, gastric lavage or induction of emesis (except in patients with impaired consciousness) and support of vital functions are advised.

The patient should be induced to vomit, even if emesis has occurred spontaneously. Pharmacologically-induced vomiting by administration of ipecac syrup is a preferred method. However, vomiting should not be induced in patients with impaired consciousness. The action of ipecac is facilitated by physical activity and by the administration of 240 to 360 mL of water. If emesis does not occur within 15 minutes, the dose of ipecac should be repeated. Precautions against aspiration should be taken, especially in children. Following emesis, adsorption of any drug remaining in the stomach may be attempted by the administration of activated charcoal as a slurry with water. If vomiting is unsuccessful, or contraindicated, gastric lavage should be performed. Physiologic saline solution is the lavage solution of choice, particularly in children. In adults, tap water can be used; however, as much as possible of the amount administered should be removed before the next instillation. Saline cathartics draw water into the bowel by osmosis and therefore may be valuable for their action in rapid dilution of bowel content. Loratadine is not removed by hemodialysis; it is not known if loratadine is removed by peritoneal dialysis.

DOSAGE AND ADMINISTRATION

Adults and Children 12 years of age and over: One loratadine tablet (10 mg), once daily.

AVAILABILITY OF DOSAGE FORMS

Each white, oval, biconvex tablet, scored and engraved 'LO' over '10' on one side and 'APO' on the other, contains 10 mg loratadine (as base). Available in bottles of 100, and unit dose blister packages of 12 and 18.

Composition

In addition to loratadine, each tablet contains the non-medicinal ingredients lactose, microcrystalline cellulose, croscarmellose sodium, magnesium stearate and colloidal silicon dioxide.

Stability and Storage Recommendations

Store at room temperature (15 to 30EC). Protect from exposure to excessive moisture.

Date of Preparation: May 25, 2001
Date of Revision: September 13, 2001