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**CLARITIN®**  
brand of loratadine  
**TABLETS, SYRUP, and**  
**RAPIDLY-DISINTEGRATING TABLETS**

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There does not appear to be any adverse clinical events in subjects who received oral contraceptives and lorazepam.

**Carcinogenesis, Mutagenesis, and Impairment of Fertility.** In an 18-month carcinogenicity study in mice and rats, 100 mg/kg/day of lorazepam was administered to 10 subjects per sex per dose group. In the 18-month oral carcinogenicity studies, pharmacokinetic assessments were carried out to determine animal exposure to the drug. AUC data demonstrated that the exposure of mice given 40 mg/kg of lorazepam was 3.5 (standard error) 18 times the exposure of mice given the maximum recommended daily oral dose. Exposure of rats given 25 mg/kg of lorazepam was 1.5 times the exposure of rats given the maximum recommended daily oral dose. Exposure of children given 25 mg/kg of lorazepam was 1.5 times the exposure of children given the maximum recommended daily oral dose. Male mice given 40 mg/kg of lorazepam were mated with females given 40 mg/kg of lorazepam. In the 18-month oral carcinogenicity studies, concurrent controls. In rats, a significantly higher incidence of hepatocellular tumors (combined adenomas and carcinomas) was observed in males given 100 mg/kg, and males and females given 25 mg/kg. Exposure of rats given 10 mg/kg of lorazepam was 0.5 times the exposure of rats given the maximum recommended daily oral dose. The exposure of rats given 20 mg/kg of lorazepam was 1.0 times the exposure of rats given the maximum recommended daily oral dose. The exposure of children given 20 mg/kg of lorazepam was 1.0 times the exposure of children given the maximum recommended daily oral dose. The exposure of children given 10 mg/kg of lorazepam was 0.5 times the exposure of children given the maximum recommended daily oral dose.

In mutagenicity studies, there was no evidence of mutagenic potential in reverse (Ames) or forward point mutation (CHO HGPRT) assays. In an assay for DNA damage, that primary hyperphosphorylated dNNA (ssDNA) or in two other hyperphosphorylated dNNA (ssDNA) assays, there was no evidence of mutagenic potential in reverse (Ames) or forward point mutation (CHO HGPRT) assays. In the mouse lymphoma assay, a positive finding occurred in the nonactivated but not in the activated group.

Dr. Falk Pharma Ex. 1089

**Pregnancy Category B:** There was no evidence of animal teratogenicity in studies performed in rats and rabbits at oral doses up to 96 mg/kg (approximately 75 times and 150 times, respectively, the maximum recommended human daily oral dose on a mg/m<sup>2</sup> basis). There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, CLARITIN should be used during pregnancy only if clearly needed.

**Nursing Mothers:** Loratadine and its metabolite, descarboethoxyloratadine, pass easily into breast milk and achieve concentrations that are equivalent to plasma levels with an AUC<sub>0-24h</sub>/AUC<sub>0-12h</sub> ratio of 1.17 and 0.85 for loratadine and descarboethoxyloratadine, respectively. Following a single oral dose of 40 mg, a small amount of loratadine and descarboethoxyloratadine was excreted into the breast milk (approximately 0.05% of 40 mg over 48 hours). A decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother. Caution should be exercised when CLARITIN is administered to a nursing woman.

**Pediatric Use:** The safety of CLARITIN Syrup at a daily dose of 10 mg has been demonstrated in 188 pediatric patients 6 to 12 years of age in placebo-controlled 2-week trials. The safety and tolerability of CLARITIN Syrup at a daily dose of 5 mg has been demonstrated in 60 pediatric patients 2 to 5 years of age in a double-blind, placebo-controlled, 2-week study. The effectiveness of CLARITIN for the treatment of seasonal allergic rhinitis and chronic idiopathic urticaria in children aged 2 to 12 years is based on an extrapolation of the demonstrated efficacy of CLARITIN in adults in these conditions and the likelihood that the disease course, pathophysiology, and the drug's effect are substantially similar to that of the adults. The recommended dose for the pediatric population is based on cross-study comparison of the pharmacokinetics of CLARITIN in adults and pediatric subjects and on the safety profile of loratadine in both adults and pediatric patients at doses equal to or higher than the recommended doses. The safety and effectiveness of CLARITIN in children under 2 years of age have not been established.

**ADVERSE REACTIONS - CLARITIN Tablets:** Approximately 90,000 patients, aged 12 and older, received CLARITIN Tablets 10 mg once daily in controlled and uncontrolled studies. Placebo-controlled clinical trials at the recommended dose of 10 mg once a day varied from 2 weeks' to 6 months' duration. The rate of premature withdrawal from these trials was approximately 2% in both the treated and placebo group.

REPORTED ADVERSE EVENTS WITH AN INCIDENCE OF MORE THAN 2% IN PLACEBO-CONTROLLED ALLERGIC RHINITIS CLINICAL TRIALS IN PATIENTS 12 YEARS OF AGE AND OLDER

| PERCENT OF PATIENTS REPORTING      |                     |                                   |                                     |
|------------------------------------|---------------------|-----------------------------------|-------------------------------------|
| LORATADINE<br>10 mg QD<br>n = 1926 | PLACEBO<br>n = 2345 | CLEMASTINE<br>1 mg BID<br>n = 536 | TERFENADINE<br>60 mg BID<br>n = 684 |
| Headache                           | 12                  | 11                                | 8                                   |
| Somnolence                         | 8                   | 6                                 | 22                                  |
| Fatigue                            | 4                   | 3                                 | 10                                  |
| Dry Mouth                          | 3                   | 2                                 | 2                                   |

Adverse events reported in placebo-controlled chronic idiopathic urticaria trials were similar to those reported in allergic rhinitis studies.

Adverse event rates did not appear to differ significantly based on age, sex, or race, although the number of nonwhite subjects was relatively small.

**CLARITIN REDITABS (loratadine rapidly-disintegrating tablets):** Approximately 500 patients received CLARITIN REDITABS (loratadine rapidly-disintegrating tablets) in controlled clinical trials of 2 weeks' duration. In these studies, adverse events were similar in type and frequency to those seen with CLARITIN Tablets and placebo.

Administration of CLARITIN REDITABS (loratadine rapidly-disintegrating tablets) did not result in an increased reporting frequency of mouth or tongue irritation.

**CLARITIN Syrup:** Approximately 300 pediatric patients 6 to 12 years of age received 10 mg loratadine once daily in controlled clinical trials for a period of 10 to 15 days. Among these, 188 children were treated with 10 mg loratadine syrup once daily in placebo-controlled trials. Adverse events in these pediatric patients were observed to occur with type and frequency similar to those seen in the adult population. The rate of premature discontinuance due to adverse events among pediatric patients receiving loratadine 10 mg daily was less than 1%.

ADVERSE EVENTS OCCURRING WITH A FREQUENCY OF ≥ 2% IN LORATADINE SYRUP-TREATED PATIENTS (6 TO 12 YEARS OLD) IN PLACEBO-CONTROLLED TRIALS, AND MORE FREQUENTLY THAN IN THE PLACEBO GROUP

| PERCENT OF PATIENTS REPORTING     |                    |                                               |
|-----------------------------------|--------------------|-----------------------------------------------|
| LORATADINE<br>10 mg QD<br>n = 188 | PLACEBO<br>n = 262 | CHLORPHENIRAMINE<br>2-4 mg BID/TID<br>n = 170 |
| Nervousness                       | 4                  | 2                                             |
| Wheezing                          | 4                  | 2                                             |
| Fatigue                           | 3                  | 2                                             |
| Hyperkinesia                      | 3                  | 1                                             |
| Abdominal Pain                    | 2                  | 0                                             |
| Constipation                      | 2                  | <1                                            |
| Dysphonia                         | 2                  | <1                                            |
| Melaise                           | 2                  | 0                                             |
| Upper Respiratory Tract Infection | 2                  | <1                                            |

Sixty pediatric patients 2 to 5 years of age received 5 mg loratadine once daily in a double-blind, placebo-controlled clinical trial for a period of 14 days. No unexpected adverse events were seen given the known safety profile of loratadine and likely adverse reactions for this patient population. The following adverse events occurred with a frequency of 2 to 3 percent in the loratadine syrup-treated patients (2 to 5 years old) during the placebo-controlled trial, and more frequently than in the placebo group: diarrhea, epistaxis, pharyngitis, influenza-like symptoms, fatigue, stomatitis, tooth disorder, sarache, viral infection, and rash.

In addition to these adverse events reported above (≥ 2%), the following adverse events have been reported in at least one patient in CLARITIN clinical trials in adult and pediatric patients:

**Autonomic Nervous System:** altered lacrimation, altered salivation, flushing, hypoesthesia, impotence, increased sweating, thirst.

**Body as a Whole:** angioneurotic edema, asthenia, back pain, blurred vision, chest pain, earache, eye pain, fever, leg cramps, malaise, rigors, limbitus, weight gain.

**Cardiovascular System:** hypertension, hypotension, palpitations, supraventricular tachyarrhythmias, syncope, tachycardia.

**Central and Peripheral Nervous System:** blepharospasm, dizziness, dysphonia, hypertension, migraine, paresthesia, tremor, vertigo.

**Gastrointestinal System:** altered taste, anorexia, constipation, diarrhea, dyspepsia, flatulence, gastritis, hiccup, increased appetite, loose stools, nausea, vomiting.

**Musculoskeletal System:** arthralgia, myalgia.

**Psychiatric:** agitation, amnesia, anxiety, confusion, decreased libido, depression, impaired concentration, insomnia, irritability, paranoia.

**Reproductive System:** breast pain, dysmenorrhea, menorrhagia, vaginitis.

**Respiratory System:** bronchitis, bronchospasm, coughing, dyspnea, hemoptysis, laryngitis, nasal dryness, sinusitis, sneezing.

**Skin and Appendages:** dermatitis, dry hair, dry skin, photosensitivity reaction, pruritis, purpura, urticaria.

**Urinary System:** altered micturition, urinary discoloration, urinary incontinence, urinary retention.

In addition, the following spontaneous adverse events have been reported rarely during the marketing of loratadine: abnormal hepatic function, including jaundice, hepatitis, and hepatic necrosis; alopecia; anaphylaxis; breast enlargement; erythema multiforme; peripheral edema; thrombocytopenia; and seizures.

**DRUG ABUSE AND DEPENDENCE:** There is no information to indicate that abuse or dependency occurs with CLARITIN.

**OVERDOSAGE:** In adults, somnolence, tachycardia, and headache have been reported with overdoses greater than 10 mg with the tablet formulation (40 mg to 160 mg). Extrapyramidal signs and palpitations have been reported in children with overdoses of greater than 10 mg of CLARITIN Syrup. In the event of overdosage, general symptomatic and supportive measures should be initiated promptly and maintained for as long as necessary.

Treatment of overdosage would reasonably consist of emesis (pecae syrup), except in patients with impaired consciousness, followed by the administration of activated charcoal to absorb any remaining drug. If vomiting is unsuccessful, or contraindicated, gastric lavage should be performed with normal saline. Saline cathartics may also be of value for rapid dilution of bowel contents. Loratadine is not eliminated by hemodialysis. It is not known if loratadine is eliminated by peritoneal dialysis.

No deaths occurred at oral doses up to 5000 mg/kg in mice (approximately 1200 and 1400 times, respectively, the maximum recommended daily oral dose in adults and children on a mg/m<sup>2</sup> basis). No deaths occurred at oral doses up to 5000 mg/kg in matured rats (approximately 2400 and 2900 times, respectively, the maximum recommended daily oral dose in adults and children on a mg/m<sup>2</sup> basis). However, lethality occurred in juvenile rats at an oral dose of 125 mg/kg (approximately 100 and 70 times, respectively, the maximum recommended daily oral dose in adults and children on a mg/m<sup>2</sup> basis). No deaths occurred at oral doses up to 1280 mg/kg in monkeys (approximately 2100 and 1500 times, respectively, the maximum recommended daily oral dose in adults and children on a mg/m<sup>2</sup> basis).

**DOSEAGE AND ADMINISTRATION:** Adults and children 6 years of age and over: The recommended dose is one 10 mg tablet or tablet, or 2 teaspoonsful (10 mg) of Syrup once daily.

Children 2 to 5 years of age: The recommended dose of CLARITIN Syrup is 5 mg (1 teaspoonful) once daily.

In adults and children 6 years of age and over with liver failure or renal insufficiency (GFR < 30 mL/min), the starting dose should be 10 mg (one tablet or two teaspoonfuls) every other day. In children 2 to 5 years of age with liver failure or renal insufficiency, the starting dose should be 5 mg (one teaspoonful) every other day.

**Administration of CLARITIN REDITABS (loratadine rapidly-disintegrating tablets):** Place CLARITIN REDITABS (loratadine rapidly-disintegrating tablets) on the tongue. Tablet disintegration occurs rapidly. Administer with or without water.

**HOW SUPPLIED - CLARITIN Tablets:** 10 mg, white to off-white compressed tablets; impressed with the product identification number "458" on one side and "CLARITIN 10" on the other; high-density polyethylene plastic bottles of 100 (NDC 0085-0458-03) and 500 (NDC 0085-0458-09). Also available, CLARITIN Unit-of-Use packages of 30 tablets (10 tablets per blister card) (NDC 0085-0458-05), and 10 x 10 tablet Unit Dose-Hospital Pack (NDC 0085-0458-04).

**Protect Unit-of-Use packaging and Unit Dose-Hospital Pack from excessive moisture.**

**Store between 2° and 30° C (36° and 86° F).**

**CLARITIN Syrup:** Clear, colorless to light-yellow liquid, containing 1 mg loratadine per mL; amber glass bottles of 16 fluid ounces (NDC 0085-1223-01).

**Store between 2° and 25° C (36° and 77° F).**

**CLARITIN REDITABS (loratadine rapidly-disintegrating tablets):** CLARITIN REDITABS (loratadine rapidly-disintegrating tablets), 10 mg, white to off-white blister-formed tablet, impressed with the letter "C" on one side; Unit-of-Use polyvinyl chloride blister packages of 30 tablets (three laminated foil pouches, each containing one blister card of 10 tablets) supplied with Patient's Instructions for Use (NDC 0085-1128-02).

**Keep CLARITIN REDITABS (loratadine rapidly-disintegrating tablets) in a dry place.**

**Store between 2° and 25° C (36° and 77° F). Use within 6 months of opening laminated foil pouch, and immediately upon opening individual tablet blister.**

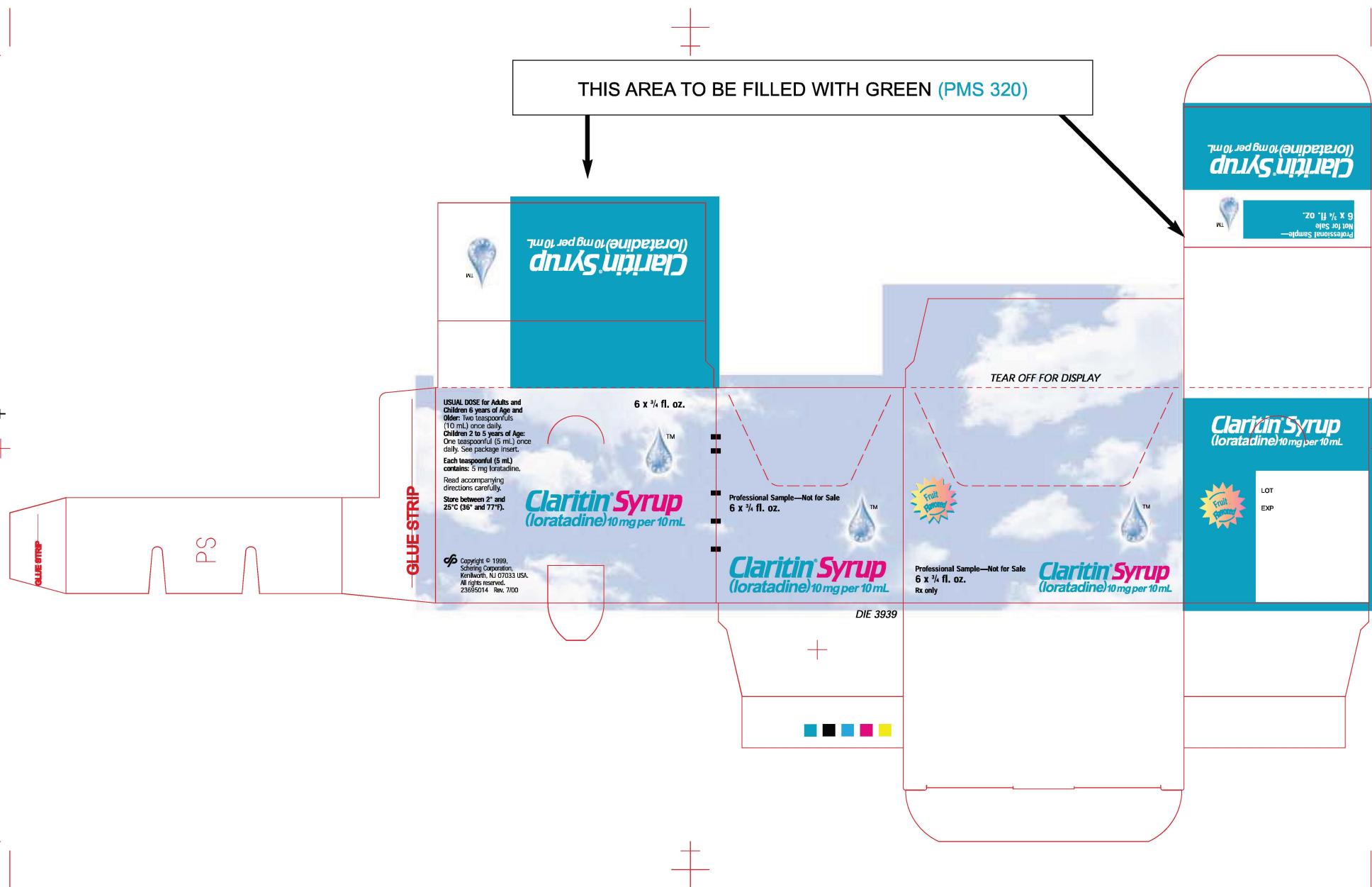
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CLARITIN REDITABS (loratadine rapidly-disintegrating tablets) are manufactured for Schering Corporation by Schere DDS, England.  
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**CLARITIN®**  
brand of loratadine  
**TABLETS, SYRUP, and**  
**RAPIDLY-DISINTEGRATING TABLETS**



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Claritin<sup>®</sup> Syrup  
(loratadine) 10 mg per 10 mL  
16 fl. oz.

DIE 3900

16 fl. oz.

Claritin<sup>®</sup> Syrup  
(loratadine) 10 mg per 10 mL



**Usual Dose for Adults and Children 6 Years of Age and Older:** Two teaspoonfuls (10 mL) once daily. **Children 2 to 5 Years of Age:** One teaspoonful (5 mL) once daily. See package insert.

**Each teaspoonful (5 mL) contains:**  
5 mg loratadine.

Read accompanying directions carefully.

Store between 2° and 25°C (36° and 77°F).

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NDC 0085-1223-01  
16 fl. oz.

Claritin<sup>®</sup> Syrup  
(loratadine) 10 mg per 10 mL



Claritin<sup>®</sup> Syrup  
(loratadine) 10 mg per 10 mL



Claritin<sup>®</sup> Syrup  
(loratadine) 10 mg per 10 mL



Schering / KEN

Rx only



PS

NDC 0085-1223-01  
16 fl. oz.

**Claritin**<sup>®</sup>  
(loratadine) **syrup**  
10 mg per 10 mL

**Rx only**

*Schering* / **KEY**

NDC 0085-1223-01  
16 fl. oz.

**Claritin**<sup>®</sup>  
(loratadine) **syrup**  
10 mg per 10 mL

**Usual Dose for Adults and Children 6 Years of Age and Older:** Two teaspoonfuls (10 mL) once daily. **Children 2 to 5 Years of Age:** One teaspoonful (5 mL) once daily. See package insert.

**Each teaspoonful (5 mL) contains:** 5 mg loratadine.

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