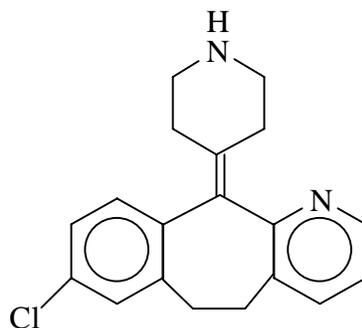


1 **CLARINEX[®]**
2 **(desloratadine)**
3 **TABLETS, REDITABS TABLETS**
4

5 **DESCRIPTION: CLARINEX** (desloratadine) Tablets are light blue, round, film
6 coated tablets containing 5 mg desloratadine, an antihistamine, to be administered
7 orally. It also contains the following excipients: dibasic calcium phosphate dihydrate
8 USP, microcrystalline cellulose NF, corn starch NF, talc USP, carnauba wax NF,
9 white wax NF, coating material consisting of lactose monohydrate, hydroxypropyl
10 methylcellulose, titanium dioxide, polyethylene glycol, and FD&C Blue # 2 Aluminum
11 Lake.

12 The CLARINEX RediTabs[®] brand of desloratadine orally-disintegrating tablets
13 is a pink colored round tablet shaped units with a "C" debossed on one side. Each
14 RediTabs unit contains 5 mg of desloratadine. It also contains the following inactive
15 ingredients: gelatin Type B NF, mannitol USP, aspartame NF, polacrillin potassium
16 NF, citric acid USP, red dye and tutti frutti flavoring.

17 Desloratadine is a white to off-white powder that is slightly soluble in water,
18 but very soluble in ethanol and propylene glycol. It has an empirical formula:
19 C₁₉H₁₉ClN₂ and a molecular weight of 310.8. The chemical name is 8-chloro-6,11-
20 dihydro-11-(4-piperidinylidene)-5H-benzo[5,6]cyclohepta[1,2-b]pyridine and has the
21 following structure :



22 **CLINICAL PHARMACOLOGY: Mechanism of Action:** Desloratadine is a long-
23 acting tricyclic histamine antagonist with selective H₁-receptor histamine antagonist
24 activity. Receptor binding data indicates that at a concentration of 2 – 3 ng/mL (7
25 nanomolar), desloratadine shows significant interaction with the human histamine
26 H₁-receptor. Desloratadine inhibited histamine release from human mast cells *in*
27 *vitro*.

28 Results of a radiolabeled tissue distribution study in rats and a radioligand H₁-
29 receptor binding study in guinea pigs showed that desloratadine did not readily cross
30 the blood brain barrier.

31 **Pharmacokinetics: Absorption:** Following oral administration of
32 desloratadine 5 mg once daily for 10 days to normal healthy volunteers, the mean
33 time to maximum plasma concentrations (T_{max}) occurred at approximately 3 hours
34 post dose and mean steady state peak plasma concentrations (C_{max}) and area under
35 the concentration-time curve (AUC) of 4 ng/mL and 56.9 ng-hr/mL were observed,
36 respectively. Neither food nor grapefruit juice had an effect on the bioavailability
37 (C_{max} and AUC) of desloratadine.

38 The pharmacokinetic profile of CLARINEX RediTabs Tablets was evaluated
39 in a three way crossover study in 30 adult volunteers. A single CLARINEX
40 RediTabs Tablet containing 5 mg of desloratadine was bioequivalent to a single 5
41 mg CLARINEX tablet and was bioequivalent to 10 mL of CLARINEX Syrup
42 containing 5 mg of desloratadine for both desloratadine and 3-hydroxydesloratadine.
43 In a separate study with 30 adult volunteers, food or water had no effect on the
44 bioavailability (AUC and C_{max}) of CLARINEX RediTabs Tablets, however, food
45 shifted the desloratadine median T_{max} value from 2.5 to 4 hr.



46 **Distribution:** Desloratadine and 3-hydroxydesloratadine are approximately 82% to
47 87% and 85% to 89%, bound to plasma proteins, respectively. Protein binding of
48 desloratadine and 3-hydroxydesloratadine was unaltered in subjects with impaired
49 renal function.

50 **Metabolism:** Desloratadine (a major metabolite of loratadine) is extensively
51 metabolized to 3-hydroxydesloratadine, an active metabolite, which is subsequently
52 glucuronidated. The enzyme(s) responsible for the formation of 3-
53 hydroxydesloratadine have not been identified. Data from clinical trials indicate that
54 a subset of the general patient population has a decreased ability to form 3-
55 hydroxydesloratadine, and are slow metabolizers of desloratadine. In
56 pharmacokinetic studies (n=1087), approximately 7% of subjects were slow
57 metabolizers of desloratadine (defined as a subject with an AUC ratio of 3-
58 hydroxydesloratadine to desloratadine less than 0.1, or a subject with a
59 desloratadine half-life exceeding 50 hours). The frequency of slow metabolizers is
60 higher in Blacks (approximately 20% of Blacks were slow metabolizers in
61 pharmacokinetic studies, n=276). The median exposure (AUC) to desloratadine in
62 the slow metabolizers was approximately 6-fold greater than the subjects who are
63 not slow metabolizers. Subjects who are slow metabolizers of desloratadine cannot
64 be prospectively identified and will be exposed to higher levels of desloratadine
65 following dosing with the recommended dose of desloratadine. Although not seen in
66 these pharmacokinetic studies, patients who are slow metabolizers may be more
67 susceptible to dose-related adverse events.

68 **Elimination:** The mean elimination half-life of desloratadine was 27 hours. C_{max} and
69 AUC values increased in a dose proportional manner following single oral doses
70 between 5 and 20 mg. The degree of accumulation after 14 days of dosing was
71 consistent with the half-life and dosing frequency. A human mass balance study
72 documented a recovery of approximately 87% of the ^{14}C -desloratadine dose, which
73 was equally distributed in urine and feces as metabolic products. Analysis of plasma
74 3-hydroxydesloratadine showed similar T_{max} and half-life values compared to
75 desloratadine.



76 **Special Populations: Geriatric:** In older subjects (≥ 65 years old; $n=17$) following
77 multiple-dose administration of CLARINEX Tablets, the mean C_{max} and AUC values
78 for desloratadine were 20% greater than in younger subjects (< 65 years old). The
79 oral total body clearance (CL/F) when normalized for body weight was similar
80 between the two age groups. The mean plasma elimination half-life of desloratadine
81 was 33.7 hr in subjects ≥ 65 years old. The pharmacokinetics for 3-
82 hydroxydesloratadine appeared unchanged in older versus younger subjects. These
83 age-related differences are unlikely to be clinically relevant and no dosage
84 adjustment is recommended in elderly subjects.

85 **Renally Impaired:** Desloratadine pharmacokinetics following a single dose of 7.5
86 mg were characterized in patients with mild ($n=7$; creatinine clearance 51-69
87 mL/min/1.73 m²), moderate ($n=6$; creatinine clearance 34-43 mL/min/1.73 m²), and
88 severe ($n=6$; creatinine clearance 5-29 mL/min/1.73 m²) renal impairment or
89 hemodialysis dependent ($n=6$) patients. In patients with mild and moderate renal
90 impairment, median C_{max} and AUC values increased by approximately 1.2- and 1.9-
91 fold, respectively, relative to subjects with normal renal function. In patients with
92 severe renal impairment or who were hemodialysis dependent, C_{max} and AUC
93 values increased by approximately 1.7- and 2.5-fold, respectively. Minimal changes
94 in 3-hydroxydesloratadine concentrations were observed. Desloratadine and 3-
95 hydroxydesloratadine were poorly removed by hemodialysis. Plasma protein
96 binding of desloratadine and 3-hydroxydesloratadine was unaltered by renal
97 impairment. Dosage adjustment for patients with renal impairment is recommended
98 (see **DOSAGE AND ADMINISTRATION** section).

99 **Hepatically Impaired:** Desloratadine pharmacokinetics were characterized following
100 a single oral dose in patients with mild ($n=4$), moderate ($n=4$), and severe ($n=4$)
101 hepatic impairment as defined by the Child-Pugh classification of hepatic function
102 and 8 subjects with normal hepatic function. Patients with hepatic impairment,
103 regardless of severity, had approximately a 2.4-fold increase in AUC as compared
104 with normal subjects. The apparent oral clearance of desloratadine in patients with
105 mild, moderate, and severe hepatic impairment was 37%, 36%, and 28% of that in
106 normal subjects, respectively. An increase in the mean elimination half-life of



107 desloratadine in patients with hepatic impairment was observed. For 3-
108 hydroxydesloratadine, the mean C_{max} and AUC values for patients with hepatic
109 impairment were not statistically significantly different from subjects with normal
110 hepatic function. Dosage adjustment for patients with hepatic impairment is
111 recommended (see **DOSAGE AND ADMINISTRATION** section).

112 **Gender:** Female subjects treated for 14 days with CLARINEX Tablets had 10% and
113 3% higher desloratadine C_{max} and AUC values, respectively, compared with male
114 subjects. The 3-hydroxydesloratadine C_{max} and AUC values were also increased by
115 45% and 48%, respectively, in females compared with males. However, these
116 apparent differences are not likely to be clinically relevant and therefore no dosage
117 adjustment is recommended.

118 **Race:** Following 14 days of treatment with CLARINEX Tablets, the C_{max} and AUC
119 values for desloratadine were 18% and 32% higher, respectively in Blacks compared
120 with Caucasians. For 3-hydroxydesloratadine there was a corresponding 10%
121 reduction in C_{max} and AUC values in Blacks compared to Caucasians. These
122 differences are not likely to be clinically relevant and therefore no dose adjustment is
123 recommended.

124 **Drug Interactions:** In two controlled crossover clinical pharmacology studies in
125 healthy male (n=12 in each study) and female (n=12 in each study) volunteers,
126 desloratadine 7.5 mg (1.5 times the daily dose) once daily was coadministered with
127 erythromycin 500 mg every 8 hours or ketoconazole 200 mg every 12 hours for 10
128 days. In 3 separate controlled, parallel group clinical pharmacology studies,
129 desloratadine at the clinical dose of 5 mg has been coadministered with
130 azithromycin 500 mg followed by 250 mg once daily for 4 days (n=18) or with
131 fluoxetine 20 mg once daily for 7 days after a 23 day pretreatment period with
132 fluoxetine (n=18) or with cimetidine 600 mg every 12 hours for 14 days (n=18) under
133 steady state conditions to normal healthy male and female volunteers. Although
134 increased plasma concentrations (C_{max} and AUC 0-24 hrs) of desloratadine and 3-
135 hydroxydesloratadine were observed (see Table 1), there were no clinically relevant
136 changes in the safety profile of desloratadine, as assessed by electrocardiographic



137 parameters (including the corrected QT interval), clinical laboratory tests, vital signs,
138 and adverse events.

139

Table 1

140 Changes in Desloratadine and 3-Hydroxydesloratadine Pharmacokinetics in Healthy
141 Male and Female Volunteers

	<u>Desloratadine</u>		<u>3-Hydroxydesloratadine</u>	
	C_{max}	AUC 0-24 hrs	C_{max}	AUC 0-24 hrs
Erythromycin (500 mg Q8h)	+ 24%	+14%	+ 43%	+ 40%
Ketoconazole (200 mg Q12h)	+ 45%	+ 39%	+ 43%	+ 72%
Azithromycin (500 mg day 1, 250 mg QD x 4 days)	+ 15%	+ 5%	+ 15%	+ 4%
Fluoxetine (20 mg QD)	+ 15%	+ 0%	+ 17%	+ 13%
Cimetidine (600 mg q12h)	+ 12%	+ 19%	- 11%	- 3%

142

143 **Pharmacodynamics: Wheal and Flare:** Human histamine skin wheal studies
144 following single and repeated 5 mg doses of desloratadine have shown that the drug
145 exhibits an antihistaminic effect by 1 hour; this activity may persist for as long as 24
146 hours. There was no evidence of histamine-induced skin wheal tachyphylaxis within
147 the desloratadine 5 mg group over the 28 day treatment period. The clinical
148 relevance of histamine wheal skin testing is unknown.

149 **Effects on QT_c:** Single dose administration of desloratadine did not alter the
150 corrected QT interval (QT_c) in rats (up to 12 mg/kg, oral), or guinea pigs (25 mg/kg,
151 intravenous). Repeated oral administration at doses up to 24 mg/kg for durations up
152 to 3 months in monkeys did not alter the QT_c at an estimated desloratadine
153 exposure (AUC) that was approximately 955 times the mean AUC in humans at the
154 recommended daily oral dose. See **OVERDOSAGE** section for information on
155 human QT_c experience.



156 **Clinical Trials:**

157 **Seasonal Allergic Rhinitis:** The clinical efficacy and safety of CLARINEX Tablets
158 were evaluated in over 2,300 patients 12 to 75 years of age with seasonal allergic
159 rhinitis. A total of 1,838 patients received 2.5 – 20 mg/day of CLARINEX in 4 double-
160 blind, randomized, placebo-controlled clinical trials of 2- to 4- weeks duration
161 conducted in the United States. The results of these studies demonstrated the
162 efficacy and safety of CLARINEX 5 mg in the treatment of adult and adolescent
163 patients with seasonal allergic rhinitis. In a dose ranging trial, CLARINEX 2.5-20
164 mg/day was studied. Doses of 5, 7.5, 10, and 20 mg/day were superior to placebo;
165 and no additional benefit was seen at doses above 5.0 mg. In the same study, an
166 increase in the incidence of somnolence was observed at doses of 10 mg/day and
167 20 mg/day (5.2% and 7.6%, respectively), compared to placebo (2.3 %).

168 In 2 four-week studies of 924 patients (aged 15 to 75 years) with seasonal
169 allergic rhinitis and concomitant asthma, CLARINEX Tablets 5 mg once daily
170 improved rhinitis symptoms, with no decrease in pulmonary function. This supports
171 the safety of administering CLARINEX Tablets to adult patients with seasonal
172 allergic rhinitis with mild to moderate asthma.

173 CLARINEX Tablets 5 mg once daily significantly reduced the Total Symptom
174 Scores (the sum of individual scores of nasal and non-nasal symptoms) in patients
175 with seasonal allergic rhinitis. See Table 2.

176 **Table 2**
177 **TOTAL SYMPTOM SCORE (TSS)**
178 **Changes in a 2 Week Clinical**
179 **Trial in Patients with Seasonal Allergic Rhinitis**

Treatment Group (n)	Mean Baseline* (sem)	Change from Baseline** (sem)	Placebo Comparison (P- value)
CLARINEX 5.0 mg (171)	14.2 (0.3)	-4.3 (0.3)	P=<0.01
Placebo (173)	13.7 (0.3)	-2.5 (0.3)	

*At baseline, a total nasal symptom score (sum of 4 individual symptoms) of at least 6 and a total non-nasal symptom score (sum of 4 individual symptoms) of at least 5 (each symptom scored 0 to 3 where 0=no symptom and 3=severe symptoms) was required for trial eligibility. TSS ranges from 0=no symptoms to 24=maximal symptoms.

**Mean reduction in TSS averaged over the 2-week treatment period.



180 There were no significant differences in the effectiveness of CLARINEX
 181 Tablets 5 mg across subgroups of patients defined by gender, age, or race.

182 **Perennial Allergic Rhinitis:** The clinical efficacy and safety of CLARINEX Tablets 5
 183 mg were evaluated in over 1,300 patients 12 to 80 years of age with perennial
 184 allergic rhinitis. A total of 685 patients received 5 mg/day of CLARINEX in 2 double
 185 blind, randomized, placebo controlled clinical trials of 4 weeks duration conducted in
 186 the United States and internationally. In one of these studies CLARINEX Tablets 5
 187 mg once daily was shown to significantly reduce symptoms of perennial allergic
 188 rhinitis (**Table 3**).

189 **Table 3**
 190 TOTAL SYMPTOM SCORE (TSS)
 191 Changes in a 4 Week Clinical
 192 Trial in Patients with Perennial Allergic Rhinitis

Treatment Group (n)	Mean Baseline* (sem)	Change from Baseline** (sem)	Placebo Comparison (P- value)
CLARINEX 5.0 mg (337)	12.37 (0.18)	-4.06 (0.21)	P=0.01
Placebo (337)	12.30 (0.18)	-3.27 (0.21)	

*At baseline, average of total symptom score (sum of 5 individual nasal symptoms and 3 non-nasal symptoms, each symptom scored 0 to 3 where 0=no symptom and 3=severe symptoms) of at least 10 was required for trial eligibility. TSS ranges from 0=no symptoms to 24=maximal symptoms.

**Mean reduction in TSS averaged over the 4-week treatment period.

193

194 **Chronic Idiopathic Urticaria:**

195 The efficacy and safety of CLARINEX Tablets 5 mg once daily was studied in 416
 196 chronic idiopathic urticaria patients 12 to 84 years of age, of whom 211 received
 197 CLARINEX. In two double-blind, placebo-controlled, randomized clinical trials of six
 198 weeks duration, at the pre-specified one-week primary time point evaluation,
 199 CLARINEX Tablets significantly reduced the severity of pruritus when compared to
 200 placebo (**Table 4**). Secondary endpoints were also evaluated and during the first
 201 week of therapy CLARINEX Tablets 5 mg reduced the secondary endpoints,
 202 "Number of Hives" and the "Size of the Largest Hive" when compared to placebo.

203

Table 4

204

PRURITUS SYMPTOM SCORE

205

Changes in the First Week of a Clinical

206

Trial in Patients with Chronic Idiopathic Urticaria

Treatment Group (n)	Mean Baseline (sem)	Change from Baseline* (sem)	Placebo Comparison (P- value)
CLARINEX 5.0 mg (115)	2.19 (0.04)	-1.05 (0.07)	P<0.01
Placebo (110)	2.21 (0.04)	-0.52 (0.07)	

Pruritus scored 0 to 3 where 0 = no symptom to 3 = maximal symptom
*Mean reduction in pruritus averaged over the first week of treatment.

207

208 **INDICATIONS AND USAGE:**

209 **Allergic Rhinitis:** CLARINEX Tablets 5 mg are indicated for the relief of the nasal
210 and non-nasal symptoms of allergic rhinitis (seasonal and perennial) in patients 12
211 years of age and older.

212 **Chronic Idiopathic Urticaria:** CLARINEX Tablets are indicated for the symptomatic
213 relief of pruritus, reduction in the number of hives, and size of hives, in patients with
214 chronic idiopathic urticaria 12 years of age and older.

215

216 **CONTRAINDICATIONS:** CLARINEX Tablets 5 mg are contraindicated in patients
217 who are hypersensitive to this medication or to any of its ingredients, or to
218 loratadine.

219

220 **PRECAUTIONS: Carcinogenesis, Mutagenesis, Impairment of Fertility:** The
221 carcinogenic potential of desloratadine was assessed using loratadine studies. In an
222 18-month study in mice and a 2-year study in rats, loratadine was administered in
223 the diet at doses up to 40 mg/kg/day in mice (estimated desloratadine and
224 desloratadine metabolite exposures were approximately 3 times the AUC in humans
225 at the recommended daily oral dose) and 25 mg/kg/day in rats (estimated
226 desloratadine and desloratadine metabolite exposures were approximately 30 times



227 the AUC in humans at the recommended daily oral dose). Male mice given 40
228 mg/kg/day loratadine had a significantly higher incidence of hepatocellular tumors
229 (combined adenomas and carcinomas) than concurrent controls. In rats, a
230 significantly higher incidence of hepatocellular tumors (combined adenomas and
231 carcinomas) was observed in males given 10 mg/kg/day and in males and females
232 given 25 mg/kg/day. The estimated desloratadine and desloratadine metabolite
233 exposures of rats given 10 mg/kg of loratadine were approximately 7 times the AUC
234 in humans at the recommended daily oral dose. The clinical significance of these
235 findings during long-term use of desloratadine is not known.

236 In genotoxicity studies with desloratadine, there was no evidence of genotoxic
237 potential in a reverse mutation assay (*Salmonella/E. coli* mammalian microsome
238 bacterial mutagenicity assay) or in two assays for chromosomal aberrations (human
239 peripheral blood lymphocyte clastogenicity assay and mouse bone marrow
240 micronucleus assay).

241 There was no effect on female fertility in rats at desloratadine doses up to 24
242 mg/kg/day (estimated desloratadine and desloratadine metabolite exposures were
243 approximately 130 times the AUC in humans at the recommended daily oral dose).
244 A male specific decrease in fertility, demonstrated by reduced female conception
245 rates, decreased sperm numbers and motility, and histopathologic testicular
246 changes, occurred at an oral desloratadine dose of 12 mg/kg in rats (estimated
247 desloratadine exposures were approximately 45 times the AUC in humans at the
248 recommended daily oral dose). Desloratadine had no effect on fertility in rats at an
249 oral dose of 3 mg/kg/day (estimated desloratadine and desloratadine metabolite
250 exposures were approximately 8 times the AUC in humans at the recommended
251 daily oral dose).

252 **Pregnancy Category C:** Desloratadine was not teratogenic in rats at doses up to
253 48 mg/kg/day (estimated desloratadine and desloratadine metabolite exposures
254 were approximately 210 times the AUC in humans at the recommended daily oral
255 dose) or in rabbits at doses up to 60 mg/kg/day (estimated desloratadine exposures
256 were approximately 230 times the AUC in humans at the recommended daily oral
257 dose). In a separate study, an increase in pre-implantation loss and a decreased



258 number of implantations and fetuses were noted in female rats at 24 mg/kg
259 (estimated desloratadine and desloratadine metabolite exposures were
260 approximately 120 times the AUC in humans at the recommended daily oral dose).
261 Reduced body weight and slow righting reflex were reported in pups at doses of 9
262 mg/kg/day or greater (estimated desloratadine and desloratadine metabolite
263 exposures were approximately 50 times or greater than the AUC in humans at the
264 recommended daily oral dose). Desloratadine had no effect on pup development at
265 an oral dose of 3 mg/kg/day (estimated desloratadine and desloratadine metabolite
266 exposures were approximately 7 times the AUC in humans at the recommended
267 daily oral dose). There are, however, no adequate and well-controlled studies in
268 pregnant women. Because animal reproduction studies are not always predictive of
269 human response, desloratadine should be used during pregnancy only if clearly
270 needed.

271 **Nursing Mothers:** Desloratadine passes into breast milk, therefore a decision
272 should be made whether to discontinue nursing or to discontinue desloratadine,
273 taking into account the importance of the drug to the mother.

274 **Pediatric Use:** The safety and effectiveness of CLARINEX Tablets in pediatric
275 patients under 12 years of age have not been established.

276 **Geriatric Use:** Clinical studies of desloratadine did not include sufficient numbers of
277 subjects aged 65 and over to determine whether they respond differently from
278 younger subjects. Other reported clinical experience has not identified differences
279 between the elderly and younger patients. In general, dose selection for an elderly
280 patient should be cautious, reflecting the greater frequency of decreased hepatic,
281 renal, or cardiac function, and of concomitant disease or other drug therapy. (see

282 **CLINICAL PHARMACOLOGY- Special Populations).**

283 **Information for Patients:** Patients should be instructed to use CLARINEX Tablets
284 as directed. As there are no food effects on bioavailability, patients can be instructed
285 that CLARINEX Tablets may be taken without regard to meals. Patients should be
286 advised not to increase the dose or dosing frequency as studies have not
287 demonstrated increased effectiveness at higher doses and somnolence may occur.



288 Phenylketonurics: CLARINEX RediTabs Tablets contain phenylalanine 1.75 mg per
 289 tablet.

290 **ADVERSE REACTIONS:**

291 **Allergic Rhinitis:** In multiple-dose placebo-controlled trials, 2,834 patients received
 292 CLARINEX Tablets at doses of 2.5 mg to 20 mg daily, of whom 1,655 patients
 293 received the recommended daily dose of 5 mg. In patients receiving 5 mg daily, the
 294 rate of adverse events was similar between CLARINEX and placebo-treated
 295 patients. The percent of patients who withdrew prematurely due to adverse events
 296 was 2.4% in the CLARINEX group and 2.6% in the placebo group. There were no
 297 serious adverse events in these trials in patients receiving desloratadine. All adverse
 298 events that were reported by greater than or equal to 2% of patients who received
 299 the recommended daily dose of CLARINEX Tablets (5.0 mg once-daily), and that
 300 were more common with CLARINEX Tablet than placebo, are listed in Table 5.

301 **Table 5**

302 Incidence of Adverse Events Reported by $\geq 2\%$ of Allergic Rhinitis Patients in
 303 Placebo-Controlled, Multiple-Dose Clinical Trials

Adverse Experience	Clarinet Tablets 5 mg (n=1,655)	Placebo (n=1,652)
Pharyngitis	4.1%	2.0%
Dry Mouth	3.0%	1.9%
Myalgia	2.1%	1.8%
Fatigue	2.1%	1.2%
Somnolence	2.1%	1.8%
Dysmenorrhea	2.1%	1.6%

304

305 The frequency and magnitude of laboratory and electrocardiographic
 306 abnormalities were similar in CLARINEX and placebo-treated patients.

307 There were no differences in adverse events for subgroups of patients as
 308 defined by gender, age, or race.

309 **Chronic Idiopathic Urticaria:** In multiple-dose, placebo-controlled trials of chronic
 310 idiopathic urticaria, 211 patients received CLARINEX Tablets and 205 received
 311 placebo. Adverse events that were reported by greater than or equal to 2% of
 312 patients who received CLARINEX Tablets and that were more common with

313 CLARINEX than placebo were (rates for CLARINEX and placebo, respectively):
314 headache (14%, 13%), nausea (5%, 2%), fatigue (5%, 1%), dizziness (4%, 3%),
315 pharyngitis (3%, 2%), dyspepsia (3%, 1%), and myalgia (3%, 1%).

316 The following spontaneous adverse events have been reported during the marketing
317 of desloratadine: tachycardia, and rarely hypersensitivity reactions (such as rash,
318 pruritus, urticaria, edema, dyspnea, and anaphylaxis), and elevated liver enzymes
319 including bilirubin.

320

321 **DRUG ABUSE AND DEPENDENCE:** There is no information to indicate that abuse
322 or dependency occurs with CLARINEX Tablets.

323

324 **OVERDOSAGE:** Information regarding acute overdose is limited to experience
325 from clinical trials conducted during the development of the CLARINEX product. In a
326 dose ranging trial, at doses of 10 mg and 20 mg/day somnolence was reported.

327 Single daily doses of 45 mg were given to normal male and female volunteers
328 for 10 days. All ECGs obtained in this study were manually read in a blinded fashion
329 by a cardiologist. In CLARINEX-treated subjects, there was an increase in mean
330 heart rate of 9.2 bpm relative to placebo. The QT interval was corrected for heart
331 rate (QT_c) by both the Bazett and Fridericia methods. Using the QT_c (Bazett) there
332 was a mean increase of 8.1 msec in CLARINEX-treated subjects relative to placebo.
333 Using QT_c (Fridericia) there was a mean increase of 0.4 msec in CLARINEX-treated
334 subjects relative to placebo. No clinically relevant adverse events were reported.

335 In the event of overdose, consider standard measures to remove any
336 unabsorbed drug. Symptomatic and supportive treatment is recommended.
337 Desloratadine and 3-hydroxydesloratadine are not eliminated by hemodialysis.

338 Lethality occurred in rats at oral doses of 250 mg/kg or greater (estimated
339 desloratadine and desloratadine metabolite exposures were approximately 120
340 times the AUC in humans at the recommended daily oral dose). The oral median
341 lethal dose in mice was 353 mg/kg (estimated desloratadine exposures were
342 approximately 290 times the human daily oral dose on a mg/m² basis). No deaths



343 occurred at oral doses up to 250 mg/kg in monkeys (estimated desloratadine
344 exposures were approximately 810 times the human daily oral dose on a mg/m²
345 basis).

346 **DOSAGE AND ADMINISTRATION:** In adults and children 12 years of age and over;
347 the recommended dose of CLARINEX Tablets is 5 mg once daily. In patients with
348 liver or renal impairment, a starting dose of one 5 mg tablet every other day is
349 recommended based on pharmacokinetic data.

350 **Administration of CLARINEX RediTabs Tablets:** Place CLARINEX
351 (desloratadine) RediTabs Tablets on the tongue. Tablet disintegration occurs
352 rapidly. Administer with or without water. Take tablet immediately after opening the
353 blister.

354 **HOW SUPPLIED: CLARINEX Tablets:** Embossed "C5", light blue film coated
355 tablets; that are packaged in high-density polyethylene plastic bottles of 100 (NDC
356 0085-1264-01) and 500 (NDC 0085-1264-02). Also available, CLARINEX Unit-of-
357 Use package of 30 tablets (3 x 10; 10 blisters per card) (NDC 0085-1264-04); and
358 Unit Dose-Hospital Pack of 100 Tablets (10 x 10; 10 blisters per card) (NDC 0085-
359 1264-03).

360

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

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

364 **Heat Sensitive. Avoid exposure at or above 30°C (86°F).**

365

366 **CLARINEX REDITABS (desloratadine orally-disintegrating tablets) 5 mg: "C"**
367 **debossed, pink tablets in foil/foil blisters.**

368 **Packs of 30 tablets (containing 3 x 10's) NDC 0085-xxxx**

369

370 **Store REDITABS TABLETS at 25° C (77°F); excursions permitted**
371 **between 15° - 30° C (59°-86°F) [See USP Controlled Room Temperature].**

372



373

374

Schering

375

Schering Corporation

376

Kenilworth, New Jersey 07033 USA

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380 06/02

XXXXXXXXXT

381

382 CLARINEX REDITABS brand of desloratadine orally-disintegrating tablets are
383 manufactured for Schering Corporation by Scherer DDS Limited, England.

384 U.S. Patent Nos. 4,659,716; 4,863,931; 4,804,666; 5,595,997; and 6,100,274

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