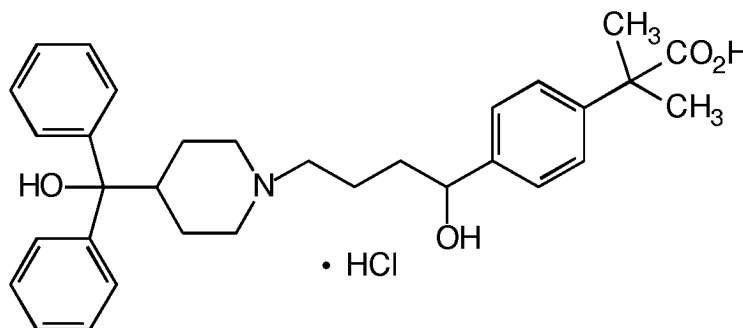


Prescribing Information as of February 2000

ALLEGRA®(fexofenadine hydrochloride) Capsules and Tablets

## DESCRIPTION

Fexofenadine hydrochloride, the active ingredient of ALLEGRA, is a histamine H<sub>1</sub>-receptor antagonist with the chemical name (±)-4-[1 hydroxy-4-[4-(hydroxydiphenylmethyl)-1-piperidiny]-butyl]-α,α-dimethyl benzeneacetic acid hydrochloride. It has the following chemical structure



The molecular weight is 538.13 and the empirical formula is C<sub>32</sub>H<sub>39</sub>NO<sub>4</sub>•HCl. Fexofenadine hydrochloride is a white to off-white crystalline powder. It is freely soluble in methanol and ethanol, slightly soluble in chloroform and water, and insoluble in hexane. Fexofenadine hydrochloride is a racemate and exists as a zwitterion in aqueous media at physiological pH.

ALLEGRA is formulated as a capsule or tablet for oral administration. Each capsule contains 60 mg fexofenadine hydrochloride and the following excipients: croscarmellose sodium, gelatin, lactose, microcrystalline cellulose, and pregelatinized starch. The printed capsule shell is made from gelatin, iron oxide, silicon dioxide, sodium lauryl sulfate, titanium dioxide, and other ingredients.

Each tablet contains 30, 60, or 180 mg fexofenadine hydrochloride (depending on the dosage strength) and the following excipients: croscarmellose sodium, magnesium stearate, microcrystalline cellulose, and pregelatinized starch. The aqueous tablet film coating is made from hydroxypropyl methylcellulose, iron oxide blends, polyethylene glycol, povidone, silicone dioxide, and titanium dioxide.

## **CLINICAL PHARMACOLOGY**

### **Mechanism of Action**

Fexofenadine hydrochloride is an antihistamine with selective peripheral H<sub>1</sub>-receptor antagonist activity. Both enantiomers of fexofenadine hydrochloride displayed approximately equipotent antihistaminic effects. Fexofenadine inhibited histamine release from peritoneal mast cells in rats. In laboratory animals, no anticholinergic, alpha<sub>1</sub>-adrenergic or beta-adrenergic-receptor blocking effects were observed. No sedative or other central nervous system effects were observed. Radiolabeled tissue distribution studies in rats indicated that fexofenadine does not cross the blood-brain barrier.

### **Pharmacokinetics**

#### **Absorption:**

Fexofenadine hydrochloride was rapidly absorbed following oral administration of a single dose of two 60 mg capsules to healthy male volunteers with a mean time to maximum plasma concentration occurring at 2.6 hours post-dose. After administration of a single 60 mg capsule to healthy subjects, the mean maximum plasma concentration was 131 ng/mL. Following single dose oral administrations of either the 60 and 180 mg tablet to healthy, adult male volunteers, mean maximum plasma concentrations were 142 and 494 ng/mL, respectively. The tablet formulations are bioequivalent to the capsule when administered at equal doses. Fexofenadine hydrochloride pharmacokinetics are linear for oral doses up to a total daily dose of 240 mg (120 mg twice daily).

#### **Distribution:**

Fexofenadine hydrochloride is 60% to 70% bound to plasma proteins, primarily albumin and α<sub>1</sub>-acid glycoprotein.

#### **Elimination:**

The mean elimination half-life of fexofenadine was 14.4 hours following administration of 60 mg, twice daily, in normal volunteers.

Human mass balance studies documented a recovery of approximately 80% and 11% of the [<sup>14</sup>C] fexofenadine hydrochloride dose in the feces and urine, respectively. Because the absolute bioavailability of fexofenadine hydrochloride has not been established, it is unknown if the fecal component represents unabsorbed drug or the result of biliary excretion.

#### **Metabolism:**

Approximately 5% of the total oral dose was metabolized.

### **Special Populations:**

Special population pharmacokinetics (for geriatric patients, renal and hepatic impairment), obtained after a single dose of 80 mg fexofenadine hydrochloride, were compared to those for normal subjects from a separate study of similar design. While subject weights were relatively uniform between studies, these adult special population patients were substantially older than the healthy, young volunteers. Thus, an age effect may be confounding the pharmacokinetic differences observed in some of the special populations.

**Seasonal allergic rhinitis (SAR) and chronic idiopathic urticaria (CIU) patients.** The pharmacokinetics of fexofenadine hydrochloride in seasonal allergic rhinitis and chronic idiopathic urticaria patients were similar to those in healthy subjects.

**Geriatric Subjects.** In older subjects ( $\geq 65$  years old), peak plasma levels of fexofenadine were 99% greater than those observed in normal volunteers ( $< 65$  years old). Mean elimination half-lives were similar to those observed in normal volunteers.

**Pediatric Patients.** Cross study comparisons indicated that fexofenadine hydrochloride area under the curve (AUC) following oral administration of a 60 mg dose to 7-12 year old pediatric allergic rhinitis patients was 56% greater compared to healthy adult subjects given the same dose. Plasma exposure in pediatric patients given 30 mg fexofenadine hydrochloride is comparable to adults given 60 mg.

**Renal Impairment.** In patients with mild to moderate (creatinine clearance 41-80 mL/min) and severe (creatinine clearance 11-40 mL/min) renal impairment, peak plasma levels of fexofenadine were 87% and 111% greater, respectively, and mean elimination half-lives were 59% and 72% longer, respectively, than observed in normal volunteers. Peak plasma levels in patients on dialysis (creatinine clearance  $\leq 10$  mL/min) were 82% greater and half-life was 31% longer than observed in normal volunteers. Based on increases in bioavailability and half-life, a dose of 60 mg once daily is recommended as the starting dose in patients with decreased renal function. (See **DOSAGE AND ADMINISTRATION**).

**Hepatic Impairment.** The pharmacokinetics of fexofenadine hydrochloride in patients with hepatic disease did not differ substantially from that observed in healthy patients.

**Effect of Gender.** Across several trials, no clinically significant gender-related differences were observed in the pharmacokinetics of fexofenadine hydrochloride.

### **Pharmacodynamics**

**Wheal and Flare.** Human histamine skin wheal and flare studies following single and twice daily doses of 20 and 40 mg fexofenadine hydrochloride demonstrated that the drug exhibits an antihistamine effect by 1 hour, achieves maximum effect at 2 to 3 hours, and an effect is still seen at 12 hours. There was no evidence of tolerance to these effects after 28 days of dosing.

Histamine skin wheal and flare studies in 7 to 12 year old patients showed that following a single dose of 30 or 60 mg, antihistamine effect was observed at 1 hour and reached a maximum by 3 hours. Greater than 49% inhibition of wheal area, and 74% inhibition of flare area were maintained for 8 hours following the 30 and 60 mg dose.

**Effects on QT<sub>c</sub>.** In dogs (30 mg/kg/ orally twice a day), and in rabbits (10 mg/kg, infused intravenously over 1 hour) fexofenadine hydrochloride did not prolong QT<sub>c</sub>. In dogs the plasma fexofenadine concentration was approximately 9 times the therapeutic plasma concentrations in adults receiving the maximum recommended daily oral dose. In rabbits, the plasma fexofenadine concentration was approximately 20 times the therapeutic plasma concentration in adults receiving the maximum recommended daily oral dose. No effect was observed on calcium channel current, delayed potassium channel current, or action potential duration in guinea pig myocytes, sodium current in rat neonatal myocytes, or on several delayed rectifier potassium channels cloned from human heart at concentrations up to  $1 \times 10^{-5}$  M of fexofenadine hydrochloride.

No statistically significant increase in mean QT<sub>c</sub> interval compared to placebo was observed in 714 seasonal allergic rhinitis patients given fexofenadine hydrochloride capsules in doses of 60 to 240 mg twice daily for two weeks. Pediatric patients from two placebo controlled trials (n=855) treated with up to 60 mg fexofenadine hydrochloride twice daily demonstrated no significant treatment or dose-related increases in QT<sub>c</sub>. In addition, no statistically significant increase in mean QT<sub>c</sub> interval compared to placebo was observed in 40 healthy volunteers given fexofenadine hydrochloride as an oral solution at doses up to 400 mg twice daily for 6 days, or in 231 healthy volunteers given fexofenadine hydrochloride 240 mg once daily for 1 year.

## **Clinical Studies**

### **Seasonal Allergic Rhinitis**

#### **Adults:**

In three, 2-week, multicenter, randomized, double-blind, placebo-controlled trials in patients 12 to 68 years of age with seasonal allergic rhinitis (n=1634), fexofenadine hydrochloride 60 mg twice daily significantly reduced total symptom scores (the sum of the individual scores for sneezing, rhinorrhea, itchy nose/palate/throat, itchy/watery/red eyes) compared to placebo. Statistically significant reductions in symptom scores were observed following the first 60 mg dose, with the effect maintained throughout the 12-hour interval. In these studies, there was no additional reduction in total symptom scores with higher doses of fexofenadine hydrochloride up to 240 mg twice daily.

In one 2-week, multi-center, randomized, double-blind clinical trial in patients 12 to 65 years of age with seasonal allergic rhinitis (n=863), fexofenadine hydrochloride 180 mg once daily significantly reduced total symptom scores (the sum of the individual scores for sneezing, rhinorrhea, itchy nose/palate/throat, itchy/watery/red eyes) compared to placebo. Although the number of patients in some of the subgroups was small, there were no significant differences in the effect of fexofenadine hydrochloride across subgroups of patients defined by gender, age, and race. Onset of action for reduction in total symptom scores, excluding nasal congestion, was observed at 60 minutes compared to placebo following a single 60 mg fexofenadine hydrochloride dose administered to patients with seasonal allergic rhinitis who were exposed to ragweed pollen in an environmental exposure unit. In one clinical trial conducted with ALLEGRA 60 mg capsules, and in one clinical trial conducted with ALLEGRA-D extended release tablets, onset of action was seen within 1 to 3 hours.

### **Pediatrics:**

Two 2-week multi-center, randomized, placebo-controlled, double-blind trials in 877 pediatric patients 6 to 11 years of age with seasonal allergic rhinitis were conducted at doses of 15, 30, and 60 mg twice daily. In one of these two studies, conducted in 411 pediatric patients, all three doses of fexofenadine hydrochloride significantly reduced total symptom scores (the sum of the individual scores for sneezing, rhinorrhea, itchy nose/palate/throat, itchy/watery/red eyes) compared to placebo, however a dose response relationship was not seen. The 60 mg twice daily dose did not provide any additional benefit over the 30 mg twice daily dose. Furthermore, exposure in pediatric patients given 30 mg fexofenadine hydrochloride is comparable to adults given 60 mg (See **CLINICAL PHARMACOLOGY**).

### **Chronic Idiopathic Urticaria:**

Two 4-week multicenter, randomized, double-blind, placebo-controlled clinical trials compared four different doses of fexofenadine hydrochloride tablet (20, 60, 120, and 240 mg twice daily) to placebo in patients aged 12 to 70 years with chronic idiopathic urticaria (n=726). Efficacy was demonstrated by a significant reduction in mean pruritus scores (MPS), mean number of wheals (MNW), and mean total symptom scores (MTSS, the sum of the MPS and MNW score). Although all four doses were significantly superior to placebo, symptom reduction was greater and efficacy was maintained over the entire 4-week treatment period with fexofenadine hydrochloride doses of  $\geq 60$  mg twice daily. However, no additional benefit of the 120 or 240 mg fexofenadine hydrochloride twice daily dose was seen over the 60 mg twice daily dose in reducing symptom scores. There were no significant differences in the effect of fexofenadine hydrochloride across subgroups of patients defined by gender, age, weight, and race.

## **INDICATIONS AND USAGE**

**Seasonal Allergic Rhinitis: ALLEGRA** is indicated for the relief of symptoms associated with seasonal allergic rhinitis in adults and children 6 years of age and older. Symptoms treated effectively were sneezing, rhinorrhea, itchy nose/palate/throat, itchy/watery/red eyes.

**Chronic Idiopathic Urticaria: ALLEGRA** is indicated for treatment of uncomplicated skin manifestations of chronic idiopathic urticaria in adults and children 6 years of age and older. It significantly reduces pruritus and the number of wheals.

## CONTRAINDICATIONS

ALLEGRA is contraindicated in patients with known hypersensitivity to any of its ingredients.

## PRECAUTIONS

### Drug interaction with erythromycin and ketoconazole:

Fexofenadine hydrochloride has been shown to exhibit minimal (ca. 5%) metabolism. However, co-administration of fexofenadine hydrochloride with ketoconazole and erythromycin led to increased plasma levels of fexofenadine hydrochloride. Fexofenadine hydrochloride had no effect on the pharmacokinetics of erythromycin and ketoconazole. In two separate studies, fexofenadine hydrochloride 120 mg twice daily (two times the recommended twice daily dose) was co-administered with erythromycin 500 mg every 8 hours or ketoconazole 400 mg once daily under steady-state conditions to normal, healthy volunteers (n=24, each study). No differences in adverse events or QT<sub>c</sub> interval were observed when patients were administered fexofenadine hydrochloride alone or in combination with erythromycin or ketoconazole. The findings of these studies are summarized in the following table:

**Effects on steady-state fexofenadine hydrochloride pharmacokinetics  
after 7 days of co-administration with fexofenadine hydrochloride  
120 mg every 12 hours (two times the recommended twice daily dose)  
in normal volunteers (n=24)**

<i>Concomitant Drug</i>	<i>C<sub>maxSS</sub> (Peak plasma concentration)</i>	<i>AUC<sub>SS(0-12h)</sub> (Extent of systemic exposure)</i>
Erythromycin (500 mg every 8 hrs)	+82%	+109%
Ketoconazole (400 mg once daily)	+135%	+164%

The changes in plasma levels were within the range of plasma levels achieved in adequate and well-controlled clinical trials.

The mechanism of these interactions has been evaluated in *in vitro*, *in situ*, and *in vivo* animal models. These studies indicate that ketoconazole or erythromycin co-administration enhances

fexofenadine gastrointestinal absorption. *In vivo* animal studies also suggest that in addition to increase absorption, ketoconazole decreases fexofenadine hydrochloride gastrointestinal secretion, while erythromycin may also decrease biliary excretion.

### **Drug Interactions with Antacids:**

Administration of 120 mg of fexofenadine hydrochloride (2 x 60 mg capsule) within 15 minutes of an aluminum and magnesium containing antacid (Maalox<sup>®</sup>) decreased fexofenadine AUC by 41% and C<sub>max</sub> by 43%. Allegra should not be taken closely in time with aluminum and magnesium containing antacids.

### **Carcinogenesis, Mutagenesis, Impairment of Fertility**

The carcinogenic potential and reproductive toxicity of fexofenadine hydrochloride were assessed using terfenadine studies with adequate fexofenadine hydrochloride exposure (based on plasma area-under-the concentration vs. time [AUC] values). No evidence of carcinogenicity was observed in an 18-month study in mice and in a 24-month study in rats at oral doses up to 150 mg/kg of terfenadine (which led to fexofenadine exposures that were respectively approximately 3 and 5 times the exposure from the maximum recommended daily oral dose of fexofenadine hydrochloride in adults and children).

In *in vitro* (Bacterial Reverse Mutation, CHO/HGPRT Forward Mutation, and Rat Lymphocyte Chromosomal Aberration assays) and *in vivo* (Mouse Bone Marrow Micronucleus assay) tests, fexofenadine hydrochloride revealed no evidence of mutagenicity.

In rat fertility studies, dose-related reductions in implants and increases in postimplantation losses were observed at an oral dose of 150 mg/kg of terfenadine (which led to fexofenadine hydrochloride exposures that were approximately 3 times the exposure of the maximum recommended daily oral dose of fexofenadine hydrochloride in adults).

### **Pregnancy**

**Teratogenic Effects: Category C.** There was no evidence of teratogenicity in rats or rabbits at oral doses of terfenadine up to 300 mg/kg (which led to fexofenadine exposures that were approximately 4 and 31 times, respectively, the exposure from the maximum recommended daily oral dose of fexofenadine in adults).

There are no adequate and well controlled studies in pregnant women. Fexofenadine should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

**Nonteratogenic Effects.** Dose-related decreases in pup weight gain and survival were observed in rats exposed to an oral dose of 150 mg/kg of terfenadine (approximately 3 times the maximum recommended daily oral dose of fexofenadine hydrochloride in adults based on comparison of fexofenadine hydrochloride AUCs).

### **Nursing Mothers**

There are no adequate and well-controlled studies in women during lactation. Because many drugs are excreted in human milk, caution should be exercised when fexofenadine hydrochloride is administered to a nursing woman.

### **Pediatric Use**

The recommended dose in patients 6 to 11 years of age is based on cross-study comparison of the pharmacokinetics of ALLEGRA in adults and pediatric patients and on the safety profile of fexofenadine hydrochloride in both adult and pediatric patients at doses equal to or higher than the recommended doses.

The safety of ALLEGRA tablets at a dose of 30 mg twice daily has been demonstrated in 438 pediatric patients 6 to 11 years of age in two placebo-controlled 2-week seasonal allergic rhinitis trials. The safety of ALLEGRA for the treatment of chronic idiopathic urticaria in patients 6 to 11 years of age is based on cross-study comparison of the pharmacokinetics of ALLEGRA in adult and pediatric patients and on the safety profile of fexofenadine in both adult and pediatric patients at doses equal to or higher than the recommended dose.

The effectiveness of ALLEGRA for the treatment of seasonal allergic rhinitis in patients 6 to 11 years of age was demonstrated in one trial (n=411) in which ALLEGRA tablets 30 mg twice daily significantly reduced total symptom scores compared to placebo, along with extrapolation of demonstrated efficacy in patients ages 12 years and above, and the pharmacokinetic comparisons in adults and children. The effectiveness of ALLEGRA for the treatment of chronic idiopathic urticaria in patients 6 to 11 years of age is based on an extrapolation of the demonstrated efficacy of ALLEGRA in adults with this condition and the likelihood that the disease course, pathophysiology and the drug's effect are substantially similar in children to that of adult patients.

The safety and effectiveness of ALLEGRA in pediatric patients under 6 years of age have not been established.

### **Geriatric Use**

Clinical studies of ALLEGRA tablets and capsules did not include sufficient numbers of subjects aged 65 years and over to determine whether this population responds differently from younger patients. Other reported clinical experience has not identified differences in responses between the geriatric and younger patients. This drug is known to be substantially excreted by the kidney, and the risk of toxic reactions to this drug may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and may be useful to monitor renal function. (See **CLINICAL PHARMACOLOGY**)



## **ADVERSE REACTIONS**

### **Seasonal Allergic Rhinitis:**

**Adults:** In placebo-controlled seasonal allergic rhinitis clinical trials in patients 12 years of age and older, which included 2461 patients receiving fexofenadine hydrochloride capsules at doses of 20 mg to 240 mg twice daily, adverse events were similar in fexofenadine hydrochloride and placebo-treated patients. All adverse events that were reported by greater than 1% of patients who received the recommended daily dose of fexofenadine hydrochloride (60 mg capsules twice daily), and that were more common with fexofenadine hydrochloride than placebo, are listed in Table 1.

In a placebo-controlled clinical study in the United States, which included 570 patients aged 12 years and older receiving fexofenadine hydrochloride tablets at doses of 120 or 180 mg once daily, adverse events were similar in fexofenadine hydrochloride and placebo-treated patients. Table 1 also lists adverse experiences that were reported by greater than 2% of patients treated with fexofenadine hydrochloride tablets at doses of 180 mg once daily and that were more common with fexofenadine hydrochloride than placebo.

The incidence of adverse events, including drowsiness, was not dose-related and was similar across subgroups defined by age, gender, and race.

**Table 1**  
**Adverse experiences in patients ages 12 years and older reported in placebo-controlled seasonal allergic rhinitis clinical trials in the United States**

**Twice daily dosing with fexofenadine capsules at rates of greater than 1%**

<i>Adverse experience</i>	<i>Fexofenadine 60 mg Twice Daily (n=679)</i>	<i>Placebo Twice Daily (n=671)</i>
Viral Infection (cold, flu)	2.5%	1.5%
Nausea	1.6%	1.5%
Dysmenorrhea	1.5%	0.3%
Drowsiness	1.3%	0.9%
Dyspepsia	1.3%	0.6%
Fatigue	1.3%	0.9%

**Once daily dosing with fexofenadine hydrochloride tablets at rates of greater than 2%**

<i>Adverse experience</i>	<i>Fexofenadine 180 mg once daily (n=283)</i>	<i>Placebo (n=293)</i>
Headache	10.6%	7.5%
Upper respiratory tract infection	3.2%	3.1%
Back pain	2.8%	1.4%

The frequency and magnitude of laboratory abnormalities were similar in fexofenadine hydrochloride and placebo-treated patients.

**Pediatric:** Table 2 lists adverse experiences in patients aged 6 to 11 years of age which were reported by greater than 2% of patients treated with fexofenadine hydrochloride tablets at a dose of 30 mg twice daily in placebo-controlled seasonal allergic rhinitis studies in the United States and Canada that were more common with fexofenadine hydrochloride than placebo.

**Table 2**  
**Adverse experiences reported in placebo-controlled seasonal allergic rhinitis studies in pediatric patients ages 6 to 11 in the United States and Canada at rates of greater than 2%**

<i>Adverse experience</i>	<i>Fexofenadine 30 mg twice daily (n=209)</i>	<i>Placebo (n=229)</i>
Headache	7.2%	6.6%
Accidental Injury	2.9%	1.3%
Coughing	3.8%	1.3%
Fever	2.4%	0.9%
Pain	2.4%	0.4%
Otitis Media	2.4%	0.0%
Upper Respiratory Tract Infection	4.3%	1.7%

**Chronic Idiopathic Urticaria:**

Adverse events reported by patients 12 years of age and older in placebo-controlled chronic idiopathic urticaria studies were similar to those reported in placebo-controlled seasonal allergic rhinitis studies. In placebo-controlled chronic idiopathic urticaria clinical trials, which included 726 patients 12 years of age and older receiving fexofenadine hydrochloride tablets at doses of 20 to 240 mg twice daily, adverse events were similar in fexofenadine hydrochloride and placebo-treated patients. Table 3 lists adverse experiences in patients aged 12 years and older which were reported by greater than 2% of patients treated with fexofenadine hydrochloride 60 mg tablets twice daily in controlled clinical studies in the United States and Canada and that were more common with fexofenadine hydrochloride than placebo. The safety of fexofenadine hydrochloride in the treatment of chronic idiopathic urticaria in pediatric patients 6 to 11 years of age is based on the safety profile of fexofenadine hydrochloride in adults and adolescent patients at doses equal to or higher than the recommended dose (See **Pediatric Use**).

**Table 3**  
**Adverse experiences reported in patients 12 years and older in placebo-controlled chronic idiopathic urticaria studies in the United States and Canada at rates of greater than 2%**

<i>Adverse experience</i>	<i>Fexofenadine 60 mg twice daily (n=186)</i>	<i>Placebo (n=178)</i>
Back pain	2.2%	1.1%
Sinusitis	2.2%	1.1%
Dizziness	2.2%	0.6%
Drowsiness	2.2%	0.0%

### **OVERDOSAGE**

Reports of fexofenadine hydrochloride overdose have been infrequent and contain limited information. However, dizziness, drowsiness, and dry mouth have been reported. Single doses of fexofenadine hydrochloride up to 800 mg (six normal volunteers at this dose level), and doses up to 690 mg twice daily for 1 month (three normal volunteers at this dose level) or 240 mg once daily for 1 year (234 normal volunteers at this dose level) were administered without the development of clinically significant adverse events as compared to placebo.

In the event of overdose, consider standard measures to remove any unabsorbed drug. Symptomatic and supportive treatment is recommended.

Hemodialysis did not effectively remove fexofenadine hydrochloride from blood (1.7% removed) following terfenadine administration.

No deaths occurred at oral doses of fexofenadine hydrochloride up to 5000 mg/kg in mice (110 times the maximum recommended daily oral dose in adults and 200 times the maximum recommended daily oral dose in children based on mg/m<sup>2</sup>) and up to 5000 mg/kg in rats (230 times the maximum recommended daily oral dose in adults and 400 times the maximum recommended daily oral dose in children based on mg/m<sup>2</sup>). Additionally, no clinical signs of toxicity or gross pathological findings were observed. In dogs, no evidence of toxicity was observed at oral doses up to 2000 mg/kg (300 times the maximum recommended daily oral dose in adults and 530 times the maximum recommended daily oral dose in children based on mg/m<sup>2</sup>).

### **DOSAGE AND ADMINISTRATION:**

### **Seasonal Allergic Rhinitis:**

*Adults and children 12 years and older:* The recommended dose of ALLEGRA is 60 mg twice daily, or 180 mg once daily. A dose of 60 mg once daily is recommended as the starting dose in patients with decreased renal function (see CLINICAL PHARMACOLOGY).

*Children 6 to 11 years:* The recommended dose of ALLEGRA is 30 mg twice daily. A dose of 30 mg once daily is recommended as the starting dose in pediatric patients with decreased renal function (see CLINICAL PHARMACOLOGY).

### **Chronic Idiopathic Urticaria:**

*Adults and children 12 years and older:* The recommended dose of ALLEGRA is 60 mg twice daily. A dose of 60 mg once daily is recommended as the starting dose in patients with decreased renal function (see CLINICAL PHARMACOLOGY).

*Children 6 to 11 years:* The recommended dose of ALLEGRA is 30 mg twice daily. A dose of 30 mg once daily is recommended as the starting dose in pediatric patients with decreased renal function (see CLINICAL PHARMACOLOGY).

### **HOW SUPPLIED**

ALLEGRA 60 mg capsules are available in: high-density polyethylene (HDPE) bottles of 60 (NDC 0088-1102-41); HDPE bottles of 100 (NDC 0088-1102-47); HDPE bottles of 500 (NDC 0088-1102-55); and aluminum-foil blister packs of 100 (NDC 0088-1102-49).

ALLEGRA capsules have a white opaque cap and a pink opaque body. The capsules are imprinted in black ink, with “ALLEGRA” on the cap and “60 mg” on the body.

ALLEGRA 30 mg tablets are available in: high-density polyethylene (HDPE) bottles of 100 (NDC 0088-1106-47) with a polypropylene screw cap containing a pulp/wax liner with heat-sealed foil inner seal and HDPE bottles of 500 (NDC 0088-1106-55) with a polypropylene screw cap containing a pulp/wax liner with heat-sealed foil inner seal.

ALLEGRA 60 mg tablets are available in: HDPE bottles of 100 (NDC 0088-1107-47) with a polypropylene screw cap containing a pulp/wax liner with heat-sealed foil inner seal; HDPE bottles of 500 (NDC 0088-1107-55) with a polypropylene screw cap containing a pulp/wax liner with heat-sealed foil inner seal; and aluminum foil-backed clear blister packs of 100 (NDC 0088-1107-49).

ALLEGRA 180 mg tablets are available in: HDPE bottles of 100 (NDC 0088-1109-47) with a polypropylene screw cap containing a pulp/wax liner with heat-sealed foil inner seal; and HDPE bottles of 500 (NDC 0088-1109-55) with a polypropylene screw cap containing a pulp/wax liner with heat-sealed foil inner seal.

ALLEGRA tablets are coated with a peach colored film coating. Tablets have the following unique identifiers: 30 mg tablets have 03 on one side and 0088 on the other; 60 mg tablets have 06 on one side and 0088 on the other; and 180 mg tablets have 018 on one side and 0088 on the other.

Store ALLEGRA capsules and tablets at controlled room temperature 20-25°C (68-77°F). (See USP Controlled Room Temperature). Foil-backed blister packs containing ALLEGRA capsules and all tablet packaging should be protected from excessive moisture.

Prescribing Information as of February 2000

Aventis Pharmaceuticals Inc. (formerly Hoechst Marion Roussel, Inc.)

Kansas City, MO 64137 USA

US Patents 4,254,129;

5,375,693; 5,578,610.

Archival NDA 20-872  
HFD-570/Div. Files  
HFD-570/J.L.Cobbs  
HFD-570/MEYER/2-25-00  
HFD-570/POOCHIKIAN/2-25-00  
HFD-570/UPPOOR  
HFD-570/WILSON/2-25-00  
HFD-570/CHOWDHURY/2-25-00  
HFD-570/HIMMEL  
HFD-570/LEE/2-25-00  
HFD-570/SANCILIO/2-25-00  
HFD-570/SUN/2-25-00  
HFD-570/ELASHOFF/2-25-00  
HFD-570/CHOI/2-25-00  
HF-2/MedWatch (with labeling)  
HFD-002/ORM (with labeling)  
HFD-102/ADRA (with labeling)  
HFD-102/Post-Marketing PM  
HFD-104/Peds/V.Kao (with labeling)  
HFD-40/DDMAC (with labeling)  
HFI-20/Press Office (with labeling)  
HFD-400/OPDRA (with labeling)  
HFD-613/OGD (with labeling)  
HFD-095/DDMS-IMT (with labeling)  
HFD-820/DNDC Division Director  
DISTRICT OFFICE

Drafted by: LCOBBS/February 16, 2000

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APPROVAL (AP)

## **POST APPROVAL TO DO LIST**

**[Please note that this page is a reminder page for the Project Manager of tasks to be performed post approval and should not be sent with the approval letter to the firm.]**

### **FOR NDAs ONLY**

- **ON THE DAY OF APPROVAL**, FAX a COPY of the Approval letter and the approved labeling text to the firm. Confirm the firm's receipt by **telephone** (NOT the FAX machine confirmation page).
- **WITHIN ONE (1) BUSINESS DAY of the confirmed receipt:**
  1. Send an E-mail to the APPROVALS distribution list with the following information
    - a. Date of approval
    - b. NDA #(s)/Supplement #(s)
    - c. Name of drug.
    - d. Name of sponsor.
    - e. Indication(s).
    - f. Dosage form/route of administration and whether this dosage form/route of administration is new.
    - g. Whether the application is for an Rx, OTC, or Rx-to-OTC switch.
    - h. Drug classification and review priority rating.

2. Place a copy of the approval letter and labeling (FPL or approved labeling text) in separate files on the CDER secure shared area (\\CDFDA\DRUGAPP). The filename convention for these two files are: #####YYY.zzz where:

##### is the NDA number

YYY is either: Altr@ for the approval letter,  
Albl@ for the approved labeling text, or  
Afpl@ for final printed labeling.

zzz is either: A.wpd@ if the document is in WordPerfect format,  
A.doc@ if the document is in MS Word format,  
A.pdf@ if the document is in Portable Document Format (PDF), or  
A.txt@ if the document is in plain text format [e.g., ANSI (for Windows) or ASCII (for DOS)]

For example: for newly approved NDA number 20-701, two files will be saved with the following filenames:

20701ltr.wpd for the approval letter in WordPerfect format  
20701lbl.pdf for the approved labeling text in PDF format



If for some reason it is not possible to place these two files on the secured shared area drive, then the document should be sent to FOI via FAX at 301-827-4576.