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Brief Summary

ALLEGRA®
(fexofenadine hydrochloride)
Capsules and Tablets

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_c 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)

Concomitant Drug	$C_{max}ss$ *(Peak plasma concentration)*	$AUC_{ss(0\text{-}12h)}$ *(Extent of systemic exposure)*
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 increasing 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®) decreased fexofenadine AUC by 41% and C_{max} 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. Three clinical safety studies comparing 15 mg BID (n=85) and 30 mg BID (n=330) of an experimental formulation of fexofenadine to placebo (n=430) have been conducted in pediatric patients aged 6 months to 5 years. In general, fexofenadine hydrochloride was well tolerated in these studies. No unexpected adverse events were seen given the known safety profile of fexofenadine and likely adverse reactions for this patient population. (See ADVERSE REACTIONS and CLINICAL PHARMACOLOGY.) The safety and effectiveness of fexofenadine hydrochloride 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%

Adverse experience	*Fexofenadine 60 mg Twice Daily (n=679)*	*Placebo Twice Daily (n=671)*
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%

Adverse experience	*Fexofenadine 180 mg once daily (n=283)*	*Placebo (n=293)*
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%

Adverse experience	*Fexofenadine 30 mg twice daily (n=209)*	*Placebo (n=229)*
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%

Three clinical safety studies in 845 children aged 6 months to 5 years comparing 15 mg BID (n=85) and 30 mg BID (n=330) of an experimental formulation of fexofenadine to placebo (n=430) have been conducted. In general, fexofenadine hydrochloride was well tolerated in these studies. No unexpected adverse events were seen given the known safety profile of fexofenadine and likely adverse reactions for this patient population. (See PRECAUTIONS Pediatric Use.) **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%

Adverse experience	*Fexofenadine 60 mg twice daily (n=186)*	*Placebo (n=178)*
Back Pain	2.2%	1.1%
Sinusitis	2.2%	1.1%
Dizziness	2.2%	0.6%
Drowsiness	2.2%	0.0%

Events that have been reported during controlled clinical trials involving seasonal allergic rhinitis and chronic idiopathic urticaria patients with incidences less than 1% and similar to placebo and have been rarely reported during postmarketing surveillance include: insomnia, nervousness, and sleep disorders or paroniria. In rare cases, rash, urticaria, pruritus and hypersensitivity reactions with manifestations such as angioedema, chest tightness, dyspnea, flushing and systemic anaphylaxis have been reported. **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^2) 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^2). 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^2). **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).

Please see product circular for full prescribing information.

Rx only
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Brief Summary
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