



BY MARY ANNE JACKSON, M.D.

identifying and treating children who have latent infection or are at risk for the disease.

We should not let the declining rate of tuberculosis in the United States lull us into missing opportunities for

Happily, the tuberculosis rate in 2006 was the lowest recorded since national reporting began in 1953. The 13,767 reported cases last year, or 4.6 per 100,000 population, represents a 3.2% decline from the rate in 2005. However, the rate of decline in TB has slowed since 2000. From 1993 through 2000, the average annual percentage decline in TB incidence was 7.3% per year. Since 2000, that rate has been just 3.8% per year, according to the latest data

from the Centers for Disease Control and Prevention (MMWR 2007;56:245-50).

Trends among children have been similar. In 2005, the latest year for which age-specific data are available, there were 863 cases among children aged 0-14 years, a rate of 1.4 per 100,000. Among those aged 15-24 years, the 1,542 cases represented a rate of 3.7 per 100,000. Both rates were slightly lower than in 2004 (1.6 and 3.8 per 100,000, respectively), and significantly less

than the 2.9 and 5.0 rates seen in 1993. But, as with the entire population, the decline has slowed among children, too.

Although the highest rates of TB in the United States are still among ethnic minorities in large urban areas, the disease is not limited to those populations. The proportion of TB cases among foreign-born individuals has increased each year since 1993; such cases now account for about one-fourth of all TB cases. In 2006, 56% of those were from five countries: Mexico, the Philippines, Vietnam, India, and China. Most of the foreign-born individuals in the United States who progress from latent TB infection to TB disease became infected while abroad. These cases represent immigrants, internationally adopted children from countries with high TB rates, and children exposed during foreign travel.

For physicians in the United States who provide primary care for children, identifying children who are at risk for TB is critical. In 2004, the American Academy of Pediatrics (AAP), the American Thoracic Society (ATS), and the CDC issued a comprehensive set of guidelines we all should follow, entitled "Targeted Tuberculin Skin Testing and Treatment of Latent Tuberculosis Infection in Children and Adolescents" (Pediatrics 2004;114:1175).

The three organizations' Pediatric Tuberculosis Collaborative Group recommended four questions to be asked about every patient:

► Was the child born outside the United States? (If yes, ask in which country. If the child was born in Africa, Asia, Latin America, or Eastern Europe, place a tuberculin skin test [TST]).

► Has the child traveled outside the United States? (If yes, ask where. If the child stayed with friends or family in any of the above-mentioned areas for a week or longer, place a TST test.)

► Has the child been exposed to anyone with TB disease? (If yes, a series of questions should follow to determine if the person had TB or latent disease, when the exposure occurred, and the nature of the contact. If exposure is confirmed, place a TST test. If the child has been in contact with someone who has TB disease, notify local health authorities and consult with an infectious disease specialist.)

► Does the child have close contact with a person who has a positive TB skin test? (Ask the same follow-up questions as in the preceding.)

The only TB test now recommended is the intradermal injection of 5 tuberculin units of purified protein derivative from *Mycobacterium tuberculosis* administered by the Mantoux technique.

The AAP/ATC/CDC guidelines define positive TST results in children and adolescents using three cutoff levels for the transverse diameter of the reaction: less than or equal to 5 mm, 10 mm, and 15 mm.

The 5-mm cutoff is used for children at high risk, including those in close contact with TB cases, those with positive findings on chest radiograph, or those with clinical evidence of TB disease.

The 10-mm cutoff is for those at mod-

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ID CONSULT

Tuberculosis Is a Pediatric Issue

Rev. October 2006a
Brief Summary

ALLEGRA® (fexofenadine hydrochloride) Tablets, 30 mg, 60 mg and 180 mg
ALLEGRA® (fexofenadine hydrochloride) Oral Suspension, 30 mg/5mL (6 mg/mL)

INDICATIONS AND USAGE

Seasonal Allergic Rhinitis

ALLEGRA tablets are indicated for the relief of symptoms associated with seasonal allergic rhinitis in adults and children 6 years of age and older. ALLEGRA Oral Suspension is indicated for the relief of symptoms associated with seasonal allergic rhinitis in children 2 to 11 years of age. Symptoms treated effectively were sneezing, rhinorrhea, itchy nose/palate/throat, itchy/watery/red eyes.

Chronic Idiopathic Urticaria

ALLEGRA tablets are indicated for treatment of uncomplicated skin manifestations of chronic idiopathic urticaria in adults and children 6 years of age and older. ALLEGRA Oral Suspension is indicated for treatment of uncomplicated skin manifestations of chronic idiopathic urticaria in children 6 months to 11 years of age.

Fexofenadine hydrochloride significantly reduces pruritus and the number of wheals.

CONTRAINDICATIONS

ALLEGRA tablets and ALLEGRA Oral Suspension are contraindicated in patients with known hypersensitivity to any of the ingredients.

PRECAUTIONS

Information for Patients

Patients and parents/caregivers of pediatric patients taking ALLEGRA tablets or suspension should receive the following information: ALLEGRA tablets or suspension are prescribed for the relief of symptoms of seasonal allergic rhinitis or for the relief of symptoms of chronic idiopathic urticaria (hives). Patients should be instructed to take ALLEGRA only as prescribed. Do not exceed the recommended dose. If any untoward effects occur while taking ALLEGRA discontinue use and consult a doctor. Do not exceed the recommended dose. The products should not be used by patients who are hypersensitive to any of the ingredients.

These products should be used in pregnancy or lactation only if the potential benefit justifies the potential risk to the fetus or nursing infant.

Patients should be advised to take the ALLEGRA tablets with water.

Patients and parents/caregivers of pediatric patients should be advised to shake the ALLEGRA Oral suspension bottle well, before each use.

Patients and parents/caregivers of pediatric patients should also be advised to store the medication in a tightly closed container in a cool, dry place, away from small children.

Drug Interaction with Erythromycin and Ketoconazole

Fexofenadine has been shown to exhibit minimal (ca. 5%) metabolism. However, co-administration of fexofenadine hydrochloride with either ketoconazole or erythromycin led to increased plasma concentrations of fexofenadine. Fexofenadine had no effect on the pharmacokinetics of either erythromycin or ketoconazole. In 2 separate studies, fexofenadine hydrochloride 120 mg twice daily (240 mg total daily dose) was co-administered with either erythromycin 500 mg every 8 hours or ketoconazole 400 mg once daily under steady-state conditions to healthy subjects (n=24, each study). No differences in adverse events or QTc interval were observed when subjects were administered fexofenadine hydrochloride alone or in combination with either erythromycin or ketoconazole. The findings of these studies are summarized in the following table.

Effects on steady-state fexofenadine 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} (Peak plasma concentration)	AUC _{0-12h} (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 vivo* animal models. These studies indicate that ketoconazole or erythromycin co-administration enhances fexofenadine gastrointestinal absorption. This observed increase in the bioavailability of fexofenadine may be due to transport-related effects, such as p-glycoprotein. *In vivo* animal studies also suggest that in addition to enhancing absorption, ketoconazole decreases fexofenadine 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.

Interactions with Fruit Juices

Fruit juices such as grapefruit, orange and apple may reduce the bioavailability and exposure of fexofenadine. This is based on the results from 3 clinical studies using histamine induced skin wheals and flares coupled with population pharmacokinetic analysis. The size of wheal and flare were significantly larger when fexofenadine hydrochloride was administered with either grapefruit or orange juices compared to water. Based on the literature reports, the same effects may be extrapolated to other fruit juices such as apple juice. The clinical significance of these observations is unknown. In addition, based on the population pharmacokinetics analysis of the combined data from grapefruit and orange juices studies with the data from a bioequivalence study, the bioavailability of fexofenadine was reduced by 36%. Therefore, to maximize the effects of fexofenadine, it is recommended that ALLEGRA tablets should be taken with water (see Pharmacokinetics and Dosage and Administration).

CARCINOGENESIS, MUTAGENESIS, IMPAIRMENT OF FERTILITY

The carcinogenic potential of fexofenadine was assessed using terfenadine studies with adequate fexofenadine 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 approximately 3 and 5 times the exposure at the maximum recommended daily oral dose of fexofenadine hydrochloride in adults [180 mg] and children [60 mg], respectively).

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 exposures that were approximately 3 times the exposure at the maximum recommended human daily oral dose of 180 mg of fexofenadine hydrochloride based on comparison of AUCs). In mice, fexofenadine hydrochloride produced no effect on male or female fertility at average oral doses up to 4438 mg/kg (which led to fexofenadine exposures that were approximately 13 times the exposure at the maximum recommended human daily oral dose of 180 mg of fexofenadine hydrochloride based on comparison of AUCs).

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 30 times, respectively, the exposure at the maximum recommended human daily oral dose of 180 mg of fexofenadine hydrochloride based on comparison of AUCs).

In mice, no adverse effects and no teratogenic effects during gestation were observed with fexofenadine hydrochloride at oral doses up to 3730 mg/kg (which led to fexofenadine exposures that were approximately 15 times the exposure at the maximum recommended human daily oral dose of 180 mg of fexofenadine hydrochloride based on comparison of AUCs).

There are no adequate and well controlled studies in pregnant women. ALLEGRA 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 (which led to fexofenadine exposures that were approximately 3 times the exposure at the maximum recommended human daily oral dose of 180 mg of fexofenadine hydrochloride based on comparison of AUCs).

NURSING MOTHERS

It is not known if fexofenadine is excreted in human milk. 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 ALLEGRA is administered to a nursing woman.

PEDIATRIC USE

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

The safety of ALLEGRA at a dose of 30 mg twice daily has been demonstrated in 438 pediatric subjects 6 years to 11 years of age in two placebo-controlled 2-week seasonal allergic rhinitis trials. The safety of ALLEGRA at doses of 15mg and 30 mg given once and twice a day has been demonstrated in 969 pediatric subjects 6 months to 5 years of age with allergic rhinitis in 3 pharmacokinetic studies and 3 safety studies. The safety of ALLEGRA for the treatment of chronic idiopathic urticaria in subjects 6 months to 11 years of age is based on cross-study comparison of the pharmacokinetics of ALLEGRA in adult and pediatric subjects and on the safety profile of fexofenadine in both adult and pediatric subjects at doses equal to or higher than the recommended dose.

The effectiveness of ALLEGRA for the treatment of seasonal allergic rhinitis in subjects 6 to 11 years of age was demonstrated in 1 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 subjects aged 12 years and older, and the pharmacokinetic comparisons in adults and children. The effectiveness of fexofenadine hydrochloride 30 mg twice daily for the treatment of seasonal allergic rhinitis in patients 2 to 5 years of age is based on the pharmacokinetic comparisons in adult and pediatric subjects and an extrapolation of the demonstrated efficacy of fexofenadine hydrochloride in adult subjects with this condition and the likelihood that the disease course, pathophysiology, and the drug's effect are substantially similar in pediatric patients to those in adult patients. The effectiveness of ALLEGRA for the treatment of chronic idiopathic urticaria in patients 6 months to 11 years of age is based on the pharmacokinetic comparisons in adults and children and 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. Administration of a 15 mg dose of fexofenadine hydrochloride to pediatric subjects 6 months to less than 2 years of age and a 30 mg dose to pediatric subjects 2 to 11 years of age produced exposures comparable to those seen with a dose of 60 mg administered to adults.

The safety and effectiveness of ALLEGRA in pediatric patients under 6 months 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 subjects. Other reported clinical experience has not identified differences in responses between the geriatric and younger subjects. 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 it 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 subjects 12 years of age and older, which included 2461 subjects receiving fexofenadine hydrochloride capsules at doses of 20 mg to 240 mg twice daily, adverse events were similar in fexofenadine hydrochloride- and placebo-treated subjects. All adverse events that were reported by greater than 1% of subjects 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 subjects 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 subjects. Table 1 also lists adverse experiences that were reported by greater than 2% of subjects 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 subjects aged 12 years and older reported in placebo-controlled seasonal allergic rhinitis clinical trials in the United States

Adverse experience	Twice-daily dosing with fexofenadine capsules at rates of greater than 1%	
	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%	0.9%
Fatigue	1.3%	0.9%

Adverse experience	Once-daily dosing with fexofenadine hydrochloride tablets at rates of greater than 2%	
	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 subjects. Pediatrics. Table 2 lists adverse experiences in subjects aged 6 years to 11 years of age which were reported by greater than 2% of subjects 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 years to 11 years in the United States and Canada at rates of greater than 2%

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

Table 3 lists adverse events in subjects 6 months to 5 years of age in 3 open single- and multiple dose pharmacokinetic studies and 3 placebo-controlled safety studies with fexofenadine hydrochloride capsule content (484 subjects) and suspension (50 subjects) at doses of 15 mg (108 subjects) and 30 mg (426 subjects) given twice a day.

Table 3
Adverse experiences reported in placebo-controlled studies in pediatric subjects with allergic rhinitis aged 6 months to 5 years of age at rates greater than 2%

Adverse experience	Fexofenadine 15 mg Twice Daily (n=108)		Fexofenadine 30 mg Twice Daily (n=426)		Total (n=534)	Placebo (n=430)
	Fexofenadine 15 mg Twice Daily (n=108)	Fexofenadine 30 mg Twice Daily (n=426)	Fexofenadine 15 mg Twice Daily (n=426)	Fexofenadine 30 mg Twice Daily (n=426)		
Vomiting	12.0%	4.2%	4.5%	5.8%	8.6%	7.0%
Pyrexia	1.9%	4.2%	3.9%	3.9%	3.9%	3.3%
Cough	1.9%	4.0%	3.6%	3.6%	3.6%	3.3%
Otitis media	2.8%	3.8%	3.6%	3.6%	3.6%	3.3%
Diarrhoea	3.7%	2.8%	3.0%	2.6%	3.0%	2.6%
Rhinorrhoea	0.9%	2.1%	1.9%	1.9%	1.9%	0.9%
Upper respiratory tract infection	0.9%	2.1%	1.9%	1.9%	1.9%	0.0%
Somnolence	2.8%	0.7%	1.1%	1.1%	1.1%	0.2%

Chronic Idiopathic Urticaria

Adverse events reported by subjects 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 subjects 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 4 lists adverse experiences in subjects aged 12 years and older which were reported by greater than 2% of subjects 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.

In a placebo-controlled clinical study in the United States, which included 167 subjects aged 12 years and older receiving fexofenadine hydrochloride 180 mg tablets, adverse events were similar in fexofenadine hydrochloride- and placebo-treated subjects. Table 4 also lists adverse experiences that were reported by greater than 2% of subjects treated with fexofenadine hydrochloride tablets at doses of 180 mg once daily 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 months to 11 years of age is based on the safety profile of fexofenadine hydrochloride in adults and pediatric patients at doses equal to or higher than the recommended dose (see Pediatric Use).

Table 4
Adverse experiences reported in subjects 12 years of age and older in placebo-controlled chronic idiopathic urticaria studies

Adverse experience	Twice-daily dosing with fexofenadine hydrochloride in studies in the United States and Canada at rates of greater than 2%	
	Fexofenadine 60 mg Twice Daily (n=191)	Placebo (n=183)
Dyspepsia	4.3%	4.4%
Myalgia	2.6%	2.2%
Back Pain	2.1%	1.1%
Dizziness	2.1%	1.1%
Pain in extremity	2.1%	0.0%

Once-daily dosing with fexofenadine hydrochloride in a study in the United States at rates of greater than 2%

Adverse experience	Fexofenadine 180 mg Once Daily (n=167)		Placebo (n=92)
	Fexofenadine 180 mg Once Daily (n=167)	Placebo (n=92)	
Headache	4.8%	3.3%	
Nasopharyngitis	2.4%	2.2%	
Upper respiratory tract infection	2.4%	2.2%	

Events that have been reported during controlled clinical trials involving seasonal allergic rhinitis and chronic idiopathic urticaria studies with incidences less than 1% and similar to placebo and have been rarely reported during postmarketing surveillance include: insomnia, nervousness, and sleep disorders or parosmia. 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 (6 healthy subjects at this dose level), and doses up to 690 mg twice daily for 1 month (5 healthy subjects at this dose level) or 240 mg once daily for 1 year (234 healthy subjects 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. Following administration of terfenadine, hemodialysis did not effectively remove fexofenadine, the major active metabolite of terfenadine, from blood (up to 1.7% removed).

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 children based on mg/m²) and up to 5000 mg/kg in rats (230 times the maximum recommended daily oral dose in adults and 210 times the maximum recommended daily oral dose in children based on mg/m²). 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 280 times the maximum recommended daily oral dose in children based on mg/m²).

DOSE AND ADMINISTRATION

ALLEGRA Tablets

Seasonal Allergic Rhinitis and Chronic Idiopathic Urticaria

Adults and Children 12 Years and Older. The recommended dose of ALLEGRA is 60 mg twice daily or 180 mg once daily with water. 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 with water. A dose of 30 mg once daily is recommended as the starting dose in pediatric patients with decreased renal function (see CLINICAL PHARMACOLOGY).

ALLEGRA Oral Suspension:

Seasonal Allergic Rhinitis

Children 2 to 11 Years: The recommended dose of ALLEGRA Oral Suspension is 30 mg twice daily. A dose of 30 mg (5 mL) once daily is recommended as the starting dose in pediatric patients with decreased renal function (see CLINICAL PHARMACOLOGY).

Chronic Idiopathic Urticaria

Children 6 Months to 11 Years: The recommended dose of ALLEGRA Oral Suspension is 30 mg (5 mL) twice daily for patients 2 to 11 years of age and 15 mg (2.5 mL) twice daily for patients 6 months to less than 2 years of age. For pediatric patients with decreased renal function, the recommended starting doses of ALLEGRA Oral Suspension are 30 mg (5 mL) once daily for patients 2 to 11 years of age and 15 mg (2.5 mL) once daily for patients 6 months to less than 2 years of age (see CLINICAL PHARMACOLOGY). Shake bottle well, before each use.

Rx only

Brief Summary of Prescribing Information Rev. October 2006a

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erate risk, including children less than 4 years of age, those with concomitant medical conditions, or those who were born in a country with a high TB prevalence.

The highest cutoff, 15 mm, is reserved for children aged 4 and older with no known risk factors.

Most physicians are familiar with the correct technique for TB testing, but fewer have had experience in interpreting the results. Guidelines suggest that the reaction must be read by a trained health care provider at 48-72 hours after placement. Interpretation should not be left to the parents. In fact, your office practice personnel may not be experienced either and, therefore, it may not be appropriate to place and read TST in the practice setting.

Evidence suggests that interpretation of TST even by health care providers may be fraught with error. In one study of 107 health care providers including 52 practicing pediatricians, 33 pediatric house officers, and 10 pediatric academicians, 93% identified a known tuberculin converter as tuberculin negative, based on their interpretation of the degree of induration. When presented with an induration of 15 mm, the group's median reading of its size was only 10 mm (Chest 1998;113:1175-7).

Live virus vaccines—measles, mumps, rubella, and varicella—can suppress the TST response. Also be aware that in patients treated with systemic corticosteroids or inpatients who have been treated with the newer tumor necrosis factor antagonists, a false-negative test result can occur, while prior receipt of the BCG vaccine—given at birth in many TB-endemic countries—can produce a false-positive result. However, most children with a history of the BCG vaccine and a positive skin test result have latent tuberculosis. In these instances, consultation with your local infectious disease specialist will be helpful.

Perhaps most important, the identification of children with latent TB infection (LTBI) or tuberculosis disease (who rarely if ever are at risk to transmit TB when less than 10 years of age) is a sentinel event that should provoke an aggressive investigation targeting adult close contacts.

Here in Kansas City, we recently had a TB outbreak in a day care center, mostly among children born in the United States, which was related to their exposure to a foreign-born adult residing in the day care home. Epidemiologic details are being investigated; a combination of problems caused by language barrier, difficulty tracing contacts, and poor record keeping in an unlicensed facility complicate the process.

The guidelines also address treatment for latent TB infection. Daily isoniazid for 9 months is the standard treatment regimen for children and adolescents without a known source case, or those with a source case known to be infected with a susceptible strain. Intermittent regimens are acceptable if given within a directly observed therapy program. Daily rifampin for 6 months is a suitable alternative for those with isoniazid-resistant/rifampin-susceptible strains, or those who can't tolerate isoniazid.

Treatment of LTBI and tuberculosis disease generally should involve the help of your local TB expert. While the proportion of TB cases resistant to both isoniazid and

rifampin remained at 1.2% from 2004 to 2005, and isoniazid remains the standard drug for LTBI treatment, we can't be complacent. In 2005, foreign-born individuals accounted for 81.5% of the 124 multidrug-resistant TB cases, and, according to the CDC, that percentage continues to grow. Treatment in such cases is more complicated, involving several drugs that are not generally used in the treatment of TB, and follow-up is important. ■

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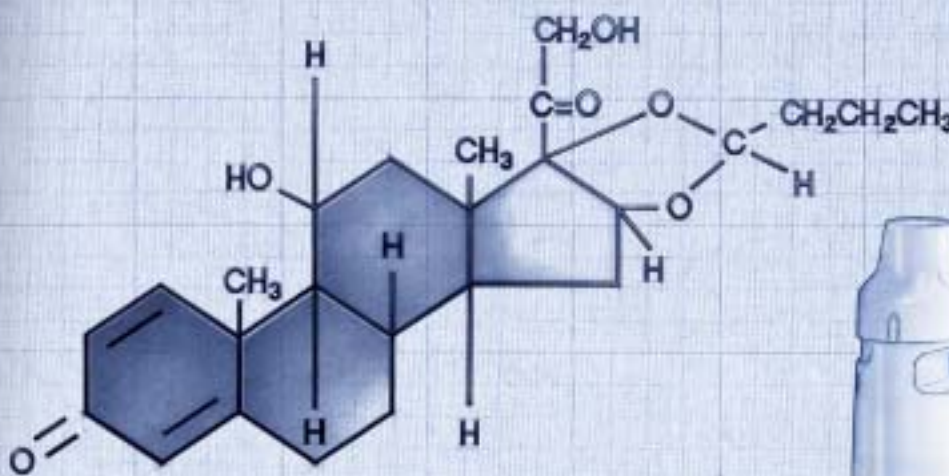
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- PULMICORT FLEXHALER™ is not a bronchodilator and is NOT indicated for the relief of acute bronchospasm
- Particular care is needed for patients who are transferred from systemically active corticosteroids to PULMICORT FLEXHALER™ because deaths due to adrenal insufficiency have occurred in asthmatic patients during and after transfer from systemic corticosteroids to less systemically available inhaled corticosteroids (see WARNINGS in Brief Summary of full Prescribing Information)
- Patients taking immunosuppressant doses of corticosteroids should avoid exposure to infections such as chicken pox and measles
- It is possible that systemic corticosteroid effects such as hypercorticism, reduced bone mineral density, and adrenal suppression may appear in a small number of patients, particularly at higher doses
- Inhaled corticosteroids may cause a reduction in growth velocity. The long-term effect on final adult height is unknown
- Rare instances of glaucoma, increased intraocular pressure, and cataracts have been reported following the inhaled administration of corticosteroids
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For more information, call 1-800-236-9933.

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