

Drugs recently approved or pending approval

TAMIFLU

The United States Food and Drug Administration approved marketing of Tamiflu (oseltamivir phosphate) by Roche Pharmaceuticals (Nutley, NJ). Tamiflu is indicated for the treatment of uncomplicated acute illness caused by influenza infection in adults who have been symptomatic for no more than 2 days. Drug efficacy was evaluated in two placebo-controlled, double-blind clinical trials. Patients with fever greater than 100°F with at least one respiratory symptom (cough, nasal symptoms, sore throat) and at least one systemic symptom (myalgia, chills/sweats, malaise, fatigue, headache) were included in the studies if influenza virus was known to be circulating in the community. Of the influenza-infected patients ($n = 849$), 95% had influenza A infection, 3% had influenza B infection, and 2% had an unknown influenza infection. Patients started treatment with Tamiflu (75 mg twice daily for 5 days) or placebo within 40 hours of symptom onset and were allowed to take fever-reducing medications. Patients self-assessed their symptoms as "none," "mild," "moderate," or "severe." Time to improvement was defined as the amount of time from treatment initiation to the time when all symptoms were assessed as none or mild. In both studies, the Tamiflu arms experienced a 1.3-day reduction in median time to improvement compared with the placebo arms. Potential adverse reactions associated with Tamiflu include nausea, vomiting, bronchitis, insomnia, and vertigo. The recommended oral dose of Tamiflu is 75 mg twice daily for 5 days.

ACCOLATE

Zeneca Pharmaceuticals (Wilmington, DE) received approval to market Accolate (zafirlukast) for the prophylaxis and long-term treatment of asthma in children age 7 years or older. Drug efficacy in pediatric patients ages 7 to 11 years was based on the demonstrated effectiveness of Accolate in adults with asthma and the probability that the disease course and the drug's effects are similar in the two populations. In one study, adults and children age 12 years and older with asthma ($n = 762$) were randomized to Accolate 20 mg twice daily ($n = 514$) or placebo ($n = 248$). Mean change in forced expiratory volume in 1 second was + 0.15 for the Accolate arm compared with + 0.05 for the placebo arm. Mean change in morning peak expiratory flow rate from baseline was + 22.06 for the Accolate arm compared with + 7.63 for the placebo arm. Drug safety in pediatric patients was evaluated in studies involving

patients ages 5 to 11 years ($n = 788$). In two double-blind trials of 4 and 6 weeks' duration, the pediatric safety profile of Accolate 10 mg twice daily compared with placebo was similar to the adult safety profile of Accolate 20 mg twice daily. Possible adverse reactions associated with pediatric use of Accolate include headache and abdominal pain. The recommended dose of Accolate for children ages 7 to 11 years is 10 mg twice daily, taken at least 1 hour before or 2 hours after meals.

TIKOSYN

The Food and Drug Administration granted approval to market Tikosyn (dofetilide) by Pfizer (New York, NY). Tikosyn is indicated for the maintenance of normal sinus rhythm (delay in time to recurrence of atrial fibrillation/atrial flutter [AF/AFL]) in patients with highly symptomatic atrial AF/AFL of greater than 1 week duration who have been converted to normal sinus rhythm and for the conversion of highly symptomatic AF/AFL to normal sinus rhythm. Drug effectiveness was evaluated in two parallel, double-blind, dose-response studies. Patients ($n = 996$) with a 1-week to 2-year history of AF/AFL were randomized to Tikosyn (125, 250, or 500 μg) or placebo twice daily. All patients started therapy in a hospital where they received continuous electrocardiographic monitoring. In one study, the percentage of patients who converted from AF/AFL to normal sinus rhythm was 6% in the 125- μg Tikosyn arm, 10% in the 250- μg Tikosyn arm, and 30% in the 500- μg Tikosyn arm, compared with 1% in the placebo arm. Of the patients who converted to normal sinus rhythm, 70% converted within 24 to 36 hours after treatment initiation. Tikosyn is contraindicated in patients with congenital or acquired long QT syndromes; patients with a baseline QT interval or QTc greater than 440 ms (500 ms in patients with ventricular conduction abnormalities); patients with severe renal impairment; and patients concomitantly taking cimetidine, verapamil, or ketoconazole. Adverse reactions associated with Tikosyn include ventricular tachycardia, headache, chest pain, and dizziness. The usual recommended dose of Tikosyn is 500 μg twice daily; however, the dose must be individualized based on calculated creatinine clearance and QTc.



Compiled from press reports and pharmaceutical company press releases. For more information, contact Deidre Yoder, Hospital Physician, 125 Strafford Avenue, Suite 220, Wayne, PA 19087-3391.