

### Drugs recently approved or pending approval

#### WELCHOL

The United States Food and Drug Administration approved marketing of Welchol (colesevelam hydrochloride) by Sankyo Parke Davis (Parsippany, NJ). Welchol is indicated alone or in combination with a hydroxymethyl-glutaryl-coenzyme A reductase inhibitor as adjunctive therapy to diet and exercise for the reduction of elevated low-density lipoprotein cholesterol (LDL-C) in patients with primary hypercholesterolemia (Frederickson Type IIa). Drug efficacy was measured in eight studies of 4 to 50 weeks' duration. Except for one long-term study, all studies were randomized, double-blind, and placebo-controlled. In one study, patients with LDL-C between 130 and 220 mg/dL received Welchol 3.8 g/day, Welchol 4.5 g/day, or placebo for 24 weeks in divided doses with the morning and evening meals. After 24 weeks, the mean LDL-C reduction was 15% in the Welchol 3.8-g arm ( $n = 95$ ) compared with 18% in the Welchol 4.5-mg arm ( $n = 94$ ) and 0% in the placebo arm ( $n = 88$ ). Welchol is contraindicated in patients with bowel obstruction. Potential adverse events associated with Welchol include flatulence, constipation, infection, headache, and pain. The recommended starting dose of Welchol as monotherapy is three 625-mg tablets taken twice daily with meals or six tablets taken once daily with a meal.



#### PROTONIX

Wyeth-Ayerst (Philadelphia, PA) received approval to market Protonix (pantoprazole sodium) delayed-release tablets for the short-term treatment (up to 8 weeks) in the healing and symptomatic relief of erosive esophagitis associated with gastroesophageal reflux disease. Efficacy of Protonix was measured in two multicenter double-blind studies. In one study, patients ( $n = 603$ ) with reflux symptoms and endoscopically diagnosed erosive esophagitis of grade 2 or higher on the Hetzel-Dent scale received Protonix (10, 20, or 40 mg/day) or placebo for 8 weeks. Approximately 25% of enrolled patients had severe erosive esophagitis of grade 3, and 10% had grade 4. The study's primary endpoint was percentage of patients healed. At week 4, healing rates were 45.6% in the 10-mg Protonix arm ( $n = 153$ ), 58.4% in the 20-mg Protonix arm ( $n = 158$ ), and 75% in the 40-mg Protonix arm ( $n = 162$ ) compared with 14.3% in the placebo arm. At week 8, the corresponding healing rates were 66%, 83.5%, 92.6%, and 39.7%. Potential adverse events associated with Protonix include headache, diarrhea, flatulence, and abdominal pain. The recommended dose

is 40 mg/day administered orally for up to 8 weeks. For patients who have not healed, an additional 8-week course of Protonix may be considered.

#### TNKASE

Approval was granted to Genentech, Inc. (South San Francisco, CA) to market TNKase (tenecteplase). TNKase is indicated for use in the reduction of mortality associated with acute myocardial infarction. Drug effectiveness was measured in an international, randomized, double-blind trial. Patients ( $n = 16,949$ ) with onset of chest pain within 6 hours of randomization and ST-segment elevation or left bundle branch block on electrocardiography were randomized to receive an intravenous (IV) bolus dose of TNKase or an accelerated infusion of alteplase recombinant, accompanied by a dose of 150 to 325 mg of aspirin administered as soon as possible, followed by 150 to 325 mg/day. IV heparin was administered based on patient weight and continued for 48 to 72 hours with infusion adjusted to maintain activated partial thromboplastin time at 50 to 75 seconds. TNKase dosage was based on actual or estimated patient weight. The study's primary endpoint was

30-day mortality rate with nonparametric adjustment for the covariates of age, Killip class, heart rate, systolic blood pressure, and infarct location. The mortality rate for patients in both the TNKase arm ( $n = 8461$ ) and the alteplase arm ( $n = 8488$ ) was 6.2%; rate of intracranial hemorrhage for both arms was 0.9%. The rate of any stroke for patients in the TNKase arm was 1.8% compared with 1.9% for patients in the alteplase arm; the rate of death or nonfatal stroke was 7.1% for patients in the TNKase arm compared with 7% for patients in the alteplase arm. TNKase is contraindicated in patients with active internal bleeding; history of cerebrovascular accident; intracranial or intraspinal surgery or trauma within 2 months; intracranial neoplasm, arteriovenous malformation, or aneurysm; known bleeding diathesis; or severe controlled hypertension. The most common adverse event associated with TNKase is bleeding. TNKase is for IV administration only. The recommended total dose should not exceed 50 mg and is based on patient weight.

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