Drugs recently approved or pending approval

BYSTOLIC

The US Food and Drug Administration (FDA) has given approval to Forest Laboratories, Inc. (St. Louis, MO) to market Bystolic (nebivolol) tablets to be used as monotherapy or in combination with other antihypertensive agents for the treatment of hypertension. The effectiveness of Bystolic monotherapy was established in 3 randomized, double-blind, multicenter, placebo-controlled trials involving 1716 patients in the general population (studies 1 and 2) and 300 black patients (study 3) with mild to moderate hypertension who had baseline diastolic blood pressures of 95 to 109 mm Hg. Patients were randomized to once-daily Bystolic 1.25 to 40 mg or placebo for 12 weeks. Bystolic used in combination with other antihypertensive agents was evaluated in a placebo-controlled study of 669 patients (mean age, 54 yr) with inadequate blood pressure control. Patients were administered Bystolic 5 to 20 mg concomitantly with up to 2 other antihypertensive agents (angiotensin–converting enzyme inhibitors, angiotensin II receptor antagonists, and thiazide diuretics). When used either as monotherapy or in combination with other antihypertensive agents, Bystolic demonstrated significant reductions in sitting diastolic and systolic blood pressure. Most studies showed increasing response to doses larger than 5 mg. The most common adverse effects associated with Bystolic were headache, fatigue, and dizziness. The recommended starting dose for most patients is 5 mg once daily.

KUVAN

BioMarin Pharmaceutical Inc. (Novato, CA) has been given FDA approval to market Kuvan (sapropterin dihydrochloride) tablets to be used in conjunction with a phenylalanine (Phe)-restricted diet to reduce blood Phe levels in patients with hyperphenylalaninemia due to tetrahydrobiopterin-responsive phenylketonuria (PKU). The efficacy and safety of Kuvan were evaluated in 4 multicenter clinical studies of patients with PKU. In study 1, an open-label, uncontrolled trial, 489 patients (aged 8–48 yr; mean age, 22 yr) who had baseline blood Phe levels of 450 µmol/L or greater and who were not on Phe-restricted diets received Kuvan 10 mg/kg/day for 8 days. At day 8, 96 patients (20%) responded to Kuvan (≥ 30% decrease in blood Phe level from baseline). In study 2 (a double-blind, placebo-controlled study), 88 patients who responded to Kuvan in study 1 were randomized to Kuvan 10 mg/kg/day or placebo for 6 weeks. The endpoint was the mean change in blood Phe level from baseline to week 6. At week 6, Kuvan-treated patients had a mean change in blood Phe level of –239 µmol/L as compared with 6 µmol/L in placebo-treated patients ($P < 0.001$). In study 3 (an open-label, extension study), 80 patients who responded to Kuvan in study 1 and completed study 2 underwent 6 weeks of forced dose-titration with 3 consecutive 2-week courses of Kuvan 5, 20, and 10 mg/kg/day. At the end of each 2-week treatment, mean blood Phe levels were 744, 640, and 581 µmol/L with 5, 10, and 20 mg/kg/day, respectively. In study 4, an open-label study, 90 children (aged 4–12 yr) who were on Phe-restricted diets and who had blood Phe levels of 480 µmol/L or less at screening were treated with Kuvan 20 mg/kg/day for 8 days. At day 8, 50 patients (56%) had at least a 30% decrease in blood Phe level from baseline. The most common adverse effects were headache, diarrhea, abdominal pain, upper respiratory tract infection, pharyngolaryngeal pain, vomiting, and nausea. The recommended starting dose of Kuvan is 10 mg/kg/day once daily.

NEXAVAR

The FDA has given approval to Bayer Pharmaceuticals Corporation (West Haven, CT) and Onyx Pharmaceuticals, Inc. (Emeryville, CA) to comarket Nexavar (sorafenib) tablets for the treatment of unresectable hepatocellular carcinoma. The safety and efficacy of Nexavar were evaluated in a phase 3, international, multicenter, randomized, double-blind, placebo-controlled trial involving 602 patients with unresectable hepatocellular carcinoma. Patients were randomized to Nexavar 400 mg twice daily or matching placebo. The primary endpoint was overall survival. Nexavar significantly improved overall survival as compared with placebo (median overall survival, 10.7 versus 7.9 mo; hazard ratio = 0.69 [95% confidence interval, 0.55–0.87]; $P = 0.001$). The most common adverse effects in patients treated with Nexavar were diarrhea, fatigue, weight loss, anorexia, nausea, and hand-foot skin reaction. The recommended daily dose is 400 mg twice daily without food. Nexavar is also indicated for the treatment of advanced renal cell carcinoma.

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

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