

Drugs recently approved or pending approval

ALDURAZYME

The US Food and Drug Administration (FDA) granted orphan drug status and approval to BioMarin Pharmaceutical Inc. (Novato, CA) and Genzyme Corporation (Cambridge, MA) to market Aldurazyme (laronidase) for the treatment of patients with the Hurler and Hurler-Scheie forms of mucopolysaccharidosis I (MPS I) and for Scheie patients with moderate to severe symptoms. MPS I is a rare, progressive disease caused by a deficiency of the enzyme alpha L-iduronidase, causing carbohydrate (ie, glycosaminoglycan) accumulation in tissue and organ systems. Aldurazyme was evaluated in a randomized, double-blind, placebo-controlled trial involving MPS I patients (N = 45). Patients received either Aldurazyme 0.58 mg/kg or placebo. All patients had a baseline forced vital capacity (FVC) less than or equal to 77% of the predicted normal and were measured on a 6-minute walk test (6MWT). After 26 weeks, patients treated with Aldurazyme showed improvement in FVC ($P = .02$) and 6MWT ($P = .07$) compared to placebo-treated patients. The most common adverse effects were upper respiratory infection, rash, and injection site reaction. Pretreatment with antipyretics and/or antihistamines is recommended 60 minutes prior to the start of Aldurazyme infusion. The total volume of the infusion is determined by the patient's body weight and should be delivered over approximately 3 to 4 hours.



IRESSA

AstraZeneca Pharmaceuticals (Wilmington, DE) received accelerated approval from the FDA to market Iressa (gefitinib) for the treatment of advanced non-small cell lung cancer (NSCLC). Iressa is indicated as monotherapy for the treatment of patients with locally advanced or metastatic NSCLC after failure of both platinum-based and docetaxel chemotherapies. Iressa was evaluated in 3 trials. A multicenter trial evaluated the tumor response rate of Iressa in patients with advanced NSCLC whose disease had progressed after at least 2 prior chemotherapy regimens including a platinum drug and docetaxel. Patients (N = 216) received Iressa 250 mg (n = 102) or 500 mg (n = 114) once daily at the same time each day. In the group receiving 250 mg/day, 13.6% (95% CI, 6.4%–24.3%) of the patients had their tumor shrink by at least 50%. The overall response rate for both doses was 10.6% (95% CI, 6.0%–16.8%). Median duration of response was 7 months (range, 4.4–18.6+ months). Iressa also was evaluated in 2 large trials of chemotherapy-naïve patients with stage III or IV NSCLC. Patients (N = 2130) were

randomized to receive Iressa 250 mg/day, Iressa 500 mg/day, or placebo, in combination with either gemcitabine and cisplatin (n = 1093) or carboplatin and paclitaxel (n = 1037). The addition of Iressa in these trials did not demonstrate any increase or trend toward increase in tumor response rates, time to progression, or overall survival; hence, Iressa is not indicated in this setting. The most common adverse effects reported with Iressa 250 mg were diarrhea, rash, acne, dry skin, nausea, and vomiting. The recommended dose of Iressa is one 250 mg tablet per day. Higher doses do not give a better response and cause increased toxicity.

VELCADE

The FDA granted accelerated approval to Millennium Pharmaceuticals Inc, of Cambridge, MA, to market Velcade (bortezomib) for the treatment of multiple myeloma patients who have received at least 2 prior therapies and have demonstrated disease progression on the last therapy. Velcade is the first of a new class of drugs known as proteasome inhibitors. The safety and efficacy of Velcade were evaluated in an open-label, single-arm, multicenter study of patients aged 34 to 84 with refractory or relapsed multiple myeloma who had at least 2 prior therapies. Patients (N = 202) were given an intravenous bolus injection of Velcade 1.3 mg/m² twice weekly for 2 weeks, followed by a 10-day rest period, for a maximum of 8 treatment cycles. The response rate for complete and partial responders was 27.7% (95% CI, 21%–35%). Complete response required fewer than 5% plasma cells in the marrow, 100% reduction in M protein, and a negative immunofixation test. The median time to response was 38 days (range, 30–127 days), and the median survival for all patients was 16 months (range, < 1 to > 18 months). The most common adverse effects reported were asthenic conditions, nausea, diarrhea, decreased appetite, constipation, thrombocytopenia, peripheral neuropathy, pyrexia, vomiting, and anemia. Therapy was discontinued in 18% of patients because of drug-related complications. The recommended dose of Velcade is 1.3 mg/m² administered as a bolus intravenous injection twice weekly for 2 weeks followed by a 10-day rest period. At least 72 hours should elapse between consecutive doses.

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