Panel Rejects Omalizumab for 6- to 11-Year-Olds

BY ELIZABETH MECHCATIE

SILVER SPRING, MD. — The majority of a Food and Drug Administration advisory panel did not support expanding the approval of omalizumab as a treatment for moderate to severe persistent asthma to include children aged 6-11 years, based on available safety and efficacy data.

The FDA's Pulmonary-Allergy Drugs Advisory Committee voted 10-4 that the safety and efficacy data on omalizumab did not provide "substantial and convincing evidence" to support approval for the proposed indication: the treatment of asthma in patients aged 6-11 years with moderate to severe persistent asthma whose symptoms are inadequately controlled with inhaled corticosteroids (ICS) and who have a positive skin test or in vitro reactivity to a perennial aeroallergen. Omalizumab, a monoclonal antibody that reduces serum IgE levels, was approved in 2003 for the same indication in adolescents and adults aged 12 years and older.

It is marketed as Xolair by Genentech USA Inc. and Novartis Pharmaceuticals.

A marginal effect on efficacy and outstanding safety issues, including concerns about long-term safety, anaphylaxis risk, and unknown implications of circulating levels of omalizumab-IgE immune complexes in some treated patients, were among the reasons panelists said they voted against approval.

Omalizumab is administered subcutaneously, every 2-4 weeks in a health care setting, at a dose based on serum IgE levels and body weight. The current label includes warnings about the potential risks of anaphylaxis and malignancies associated with treatment, based on data in clinical trials and postmarketing reports. In July 2009, the FDA reported that a cardiovascular safety signal associated with omalizumab was identified in post-marketing reports.

Omalizumab was evaluated in a pivotal 52-week study of 627 children aged 6-11 years with moderate to severe persistent, inadequately controlled allergic asthma, despite treatment with fluticasone at a dose of 200 mcg or more per day (or the equivalent), with or without other controller medications, which included short-acting beta-agonists (a mean of 2.8 puffs/day) and leukotriene antagonists (37%).

Panelists had concerns about the agent's long-term safety, anaphylaxis risk, and unknown implications of circulating omalizumab-IgE immune complexes in some patients.

The primary end point, the rate of clinically significant asthma exacerbations (defined as worsening of symptoms requiring a doubling of the baseline ICS dose for 3 days or more and/or treatment with rescue systemic intravenous or oral steroids for 3 days) at 24 weeks, was 0.45 among those treated with omalizumab, compared with 0.64 among those on placebo, which was statistically significant.

One secondary efficacy end point, the asthma exacerbation rate at 52 weeks, was significant in favor of omalizumab (0.78 among those on omalizumab, compared with 1.30 among those on placebo).

The other secondary end points—nocturnal symptom scores, asthma medication rescue use, and quality of life scores at 24 weeks—were not significantly different between the two groups. The most common adverse effects in pediatric studies were nasopharyngitis, upper respiratory tract infections, and headache; these were reported at similar rates in those on placebo and omalizumab.

No new safety signals were identified, and there were no malignancies among omalizumab-treated patients. The one case of anaphylaxis in an omalizumab-treated patient was associated with a meperidine hydrochloride (Demerol) injection.

The FDA usually follows the recommendations of its advisory panels. ■