FDA Panel OKs Antibiotic For *Pseudomonas* in CF

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GAITHERSBURG, MD. — Studies of an inhaled formulation of the monobactam antibiotic aztreonam in patients with cystic fibrosis show that it is a safe and effective treatment for *Pseudomonas aeruginosa* lung infections in this population, most of a federal advisory panel agreed.

The Food and Drug Administration's Anti-Infective Drugs Advisory Committee voted 15-2 that the manufacturer, Gilead Sciences Inc., had provided substantial evidence that inhaled aztreonam, administered at a dose of 75 mg three times a day for 28 days, was safe and effective for the proposed indication: the improvement of respiratory symptoms and pulmonary function in patients who have cystic fibrosis (CF) with *P. aeruginosa*.

If aztreonam lysine for inhalation (AZLI) is approved, the company plans to market it as Cayston, with a novel, portable handheld nebulizer that delivers the 75-mg dose in 2-3 minutes. The panel was not asked to specifically vote on whether to recommend approval.

Inhaled aztreonam has already been approved for this indication in the European Union, Canada, and other countries. The intravenous formulation was approved in 1986 in the United States for indications that include *P. aeruginosa* infections, but not specifically for CF patients.

Although the FDA raised issues about whether 75 mg three times a day was the best dose, the panel unanimously agreed in a 17-0 vote that this dose had been shown to be safe and effective, although several panelists said that other doses should be studied.

AZLI was compared with placebo in two pivotal placebo-controlled phase III studies of patients aged 6 years and older with CF (mean age was in the mid-20s to early-30s), who had *P. aeruginosa* and forced expiratory volume in 1 second (FEV_1) of 25%-75% (predicted).

In one study, approximately 200 patients received 75 mg of AZLI or placebo twice or three times a day for 28 days, after completing 28 days of treatment with tobramycin inhalation solution (TOBI), the only FDA-approved inhaled antibiotic approved for treating *P. aeruginosa* in CF patients (approved in 1997). The primary end point—the time to need for inhaled or intravenous antipseudomonal antibiotics from the time they started AZLI or placebo—was a median of 92 days among those on AZLI, compared with a median of 71 days among those on placebo, a significant difference. Those on AZLI also had improvements in FEV_1, a secondary end point; these improvements were significantly greater than they were in those on placebo.

In a second study, which enrolled 164 patients treated with AZLI or placebo three times a day for 28 days, the primary end point was the change from day 0 to 28 in clinical symptoms, as assessed by the respiratory scores of a CF symptom questionnaire. In both studies, AZLI-treated patients also had significantly better mean changes in FEV_1 over a period of 28 days, a secondary end point, when compared with those on placebo.

The FDA usually follows the recommendations of its advisory panels, which are not binding. ■