

# Pediatric News

THE LEADER  
IN NEWS  
AND  
MEETING  
COVERAGE

# #1

Thanks For  
Making Us

Source: PERQ/HCI Corp., Focus® Medical/Surgical June 2009 Readership Summary; Pediatrics Section, Tables 1001 and 1002 Projected Average Issue Readers

## FDA Panel OKs Antibiotic For *Pseudomonas* in CF

BY ELIZABETH MEHCATIE

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<sub>1</sub>) 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<sub>1</sub>, 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<sub>1</sub> 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. ■

# Deflux®

## Stop Febrile UTIs in Their Tracts

For a list of pediatric urologists in your area who use Deflux, visit [www.deflux.com](http://www.deflux.com).

### Intended Use/Indications

Deflux® is indicated for treatment of children with vesicoureteral reflux (VUR) grades II-IV.

### Contraindications

Deflux is contraindicated in patients with any of the following conditions:

- Non-functional kidney(s)
- Hutch diverticuli
- Ureterocele
- Active voiding dysfunction
- Ongoing urinary tract infection

### Warnings

- Do not inject Deflux intravascularly. Injection of Deflux into blood vessels may cause vascular occlusion.

### Precautions

- Deflux should only be administered by qualified physicians experienced in the use of a cystoscope and trained in subureteral injection procedures.
- The risks of infection and bleeding are associated with the cystoscopic procedure used to inject Deflux.
- The usual precautions associated with cystoscopy (e.g. sterile technique, proper dilation, etc.) should be followed.
- The safety and effectiveness of the use of more than 6 ml of Deflux (3 ml at each ureteral orifice) at the same treatment session have not been established.
- The safety and effectiveness of Deflux in the treatment of children under 1 year of age have not been established.

### Adverse Events

List of treatment-related adverse events for 39 patients from a randomized study and 170 patients from nonrandomized studies. (Follow-up for studies was 12 months).

Adverse Event Category	Randomized Study (n=39 DEFLUX patients)	Nonrandomized Studies (n=170 DEFLUX patients)
UTI(i)	6 (15.4%) (ii, iii)	13 (7.6%) (ii, iii)
Ureteral dilation (iv)	1 (2.6%)	6 (3.5%)
Nausea/Vomiting/Abdominal pain (v)	0 (0%)	2 (1.2%)

- (i) Cases of UTI typically occurred in patients with persistent reflux.
- (ii) Patients in the nonrandomized studies received antibiotic prophylaxis until the 3-month VCUG. After that only those patients whose treatment had failed received further antibiotic prophylaxis. The patients in the randomized study received antibiotic prophylaxis 1 month post-treatment.
- (iii) All UTI cases were successfully treated with antibiotics.
- (iv) No case of ureteral dilation required intervention and most cases resolved spontaneously.
- (v) Both cases of nausea/vomiting/abdominal pain were resolved.

Although vascular occlusion, ureteral obstruction, dysuria, hematuria/bleeding, urgency and urinary frequency have not been observed in any of the clinical studies, they are potential adverse events associated with subureteral injection procedures. Following approval, rare cases of post-operative dilation of the upper urinary tract with or without hydronephrosis leading to temporary placement of a ureteric stent have been reported.

**References:** 1. American Academy of Pediatrics. Committee on Quality Improvement, Subcommittee on Urinary Tract Infection. Practice parameter. The diagnosis, treatment, and evaluation of the initial urinary tract infection in febrile infants and young children. *Pediatrics*. 1999;103(4):843-852. 2. Elder JS, Shah MB, Batiste LR, Eaddy M. Part 3: endoscopic injection versus antibiotic prophylaxis in the reduction of urinary tract infections in patients with vesicoureteral reflux. In: Hensle TW. Challenges surrounding vesicoureteral reflux: fuel for a paradigm shift in treatment. *Curr Med Res Opin*. 2007;23(suppl 4):S15-S20. 3. Chi A, Gupta A, Snodgrass W. Urinary tract infection following successful dextranomer/hyaluronic acid injection for vesicoureteral reflux. *J Urol*. 2008;179:1966-1969. 4. Elmore JM, Kirsch AJ, Heiss EA, Gilchrist A, Scherz HC. Incidence of urinary tract infections in children after successful ureteral reimplantation versus endoscopic dextranomer/hyaluronic acid implantation. *J Urol*. 2008;179:2364-2368. 5. Cerwinka WH, Scherz HC, Kirsch AJ. Endoscopic treatment of vesicoureteral reflux with dextranomer/hyaluronic acid in children. *Adv Urol*. Published Online: May 14, 2008 (doi:10.1155/2008/513854). 6. DEFLUX® [Package Insert]. Edison, NJ: Oceana Therapeutics (US), Inc; 2009. 7. Data on file. Oceana Therapeutics (US), Inc.

Deflux is a registered trademark of Q-Med AB.

Oceana®  
Therapeutics, Inc.

©2010 Oceana Therapeutics, Inc.

All rights reserved.

Printed in the USA.

D120925