

APPEAL TO FDA FOR APPROVAL OF INHALED AZTREONAM TALKING POINTS FOR ADVOCACY

Background: On September 16, 2008 Gilead Sciences announced that the FDA had sent notification that they could not approve the application for inhaled aztreonam lysine in its current form and that an additional clinical study will be required. In the large Phase III trial, positive, statistically significant clinical results were demonstrated as was safety, yet the FDA review committee, which recently underwent a complete turnover in staff, asked for more details. Gilead plans to appeal this decision. The implications of this delay – and possible denial – are huge, both to the community in need of alternative treatments in the short term, and to the drug development process for other CF drugs. It is very important that the CF community alert legislators to facilitate reconsideration of this decision. A further delay could bring the development of other CF and even other “orphan disease” drugs to a halt, in view of the current economy and the relatively small but growing patient population that stands to benefit.

Call to Action: Ask your legislators (congress, senators) to contact the director of the FDA and others in the administration to allow this drug to move forward. Legislators’ contact information can be found at: <http://www.visi.com/juan/congress/>

Talking Points: There are four primary reasons why this is such an important issue to people with cystic fibrosis, their families, their employers and other people with orphan drugs:

- 1. Patients have very few treatment options.** Patients need alternatives if they have developed a resistance to - or a reduced tolerance of - a current drug therapy. Otherwise, they face more frequent hospitalizations and more frequent, multiple intravenous antibiotics. The large Phase III aztreonam trial showed safety, reduced hospitalizations, improved quality of life and improved lung function.
- 2. Increasing the cost & risk of drug development.** Cystic fibrosis is an orphan disease, with a growing adult population. In recent years there has been a renaissance of interest in new treatments. However, clinical trials are extremely expensive. If the FDA sets higher hurdles for *drugs that are already approved for use in other formulations*, many of the small (and even large) companies that have been working on inhaled formulations of existing drugs may choose not to deploy their limited funding to an orphan drug. *None of the other inhaled antibiotics being developed are yet in Phase III trials.* The recent economic downturn coupled with more extensive testing hurdles could kill many of these new formulations, many of which could mean more, and more productive, years of life to thousands of adults with cystic fibrosis. The FDA’s role is to protect the public, yet there were *no safety concerns* cited in the review, hence approval of inhaled aztreonam would not compromise public safety. However, failure to approve a drug could compromise the health of persons with severe cystic fibrosis. The FDA’s message in this case could have strong, negative repercussions across the entire cystic fibrosis drug development spectrum.
- 3. New inhaled antibiotics are cost effective.** Inhaled aztreonam was shown to reduce hospitalizations and time on intravenous therapy, both very expensive treatment options. Furthermore, inhaled antibiotics improve working CF adults’ abilities to manage work (and stay off disability). Effective medications reduce hospitalization costs, disability costs, and employer costs.
- 4. Limited resources stretched thin.** A final more subtle consequence of the FDA request for another trial is the human opportunity cost of clinical trials. The Phase III trial enrolled 246 patients. There are far more clinical trials in need of patients than the very limited number of adults with cystic fibrosis who meet study criteria. Running another clinical trial for aztreonam – when the original trial showed *no safety concerns* and significant positive results – reduces the pool of patients for other trials – and therefore slows the drug development process in cystic fibrosis for this drug *and* others. The FDA needs to be acutely aware of the finite human resources available for testing these drugs, particularly when no safety issues are at stake.

The Bottom Line: The FDA must reconsider its position on inhaled aztreonam in view of 1) the urgent need for new treatment options for persons with severe cystic fibrosis lung disease; 2) in the interest of the quality of life, cost of health care and disability of individuals with cystic fibrosis, and 3) for the future of drug development for persons with cystic fibrosis and other orphan diseases.

Studies: [Am J Respir Crit Care Med.](#) 2008 Nov 1;178(9):921-8. Epub 2008 Jul 24
[Pediatr Pulmonol.](#) 2008 Jan;43(1):47-58
[Pediatr Pulmonol.](#) 2006 Jul;41(7):656-65