OFFICE OF CLINICAL PHARMACOLOGY REVIEW

NDA:	201-820
Submission Date(s):	April 12, 2011
Proposed Brand Name	Bethkis
Generic Name	Tobramycin
Primary Reviewer	Ryan Owen, Ph.D.
Team Leader	Kimberly Bergman, Pharm.D.
OCP Division	DCP4
OND Division	DAIOP
Applicant	Chiesi
Relevant IND(s)	72,068
Submission Type; Code	Original 505(b)(2) ; Type 5 (New Formulation) ; Resubmission
Formulation; Strength(s)	Tobramycin 300 mg/4 mL Inhalation Solution
Indication	For the management of cystic fibrosis patients with *Pseudomonas aeruginosa.*

BACKGROUND

CHF 1538, a tobramycin solution for nebulization (300 mg/4 mL unit dose ampule) differs from the currently marketed TOBI® (300 mg/5 mL unit dose ampule) in concentration per mL, osmolarity, and pH. CHF1538 has been approved in Europe since 2006, and is marketed as Bramitob® in 15 countries for the long-term management of chronic pulmonary infections caused by *Pseudomonas aeruginosa* in cystic fibrosis (CF) patients six years of age and older.

A 505(b)(2) NDA in support of CHF 1538 for the management of CF patients with *Pseudomonas aeruginosa* was originally submitted on 10/22/10. The original NDA received a complete response letter on 8/25/11 due to concerns about linking the proposed to-be-marketed nebulizer/compressor combination to what was used in the clinical trials, issues with the pulmonary function test data, and several device-related concerns. There were no clinical pharmacology concerns in the complete response letter.

The clinical pharmacology review for the initial NDA submission was written by Dr. Yongheng Zhang (in DARRTS under NDA 201-820, submitted on 6/30/11). This review details all of the clinical pharmacology-related studies that were conducted in support of the initial NDA. Dr. Zhang recommended approval of the original NDA from a clinical pharmacology standpoint. On 4/12/12, the Sponsor re-submitted their NDA. There was no new clinical pharmacology information contained in the resubmission. Therefore, this review is limited to labeling recommendations. The proposed label is included in this review complete with clinical pharmacology recommendations shown as track changes. Please refer to Dr. Zhang's 6/30/11 review for all supporting clinical pharmacology information.

RECOMMENDATION

The Clinical Pharmacology information provided by the Sponsor in the NDA submission is acceptable.

18 Page(s) of Draft Labeling have been Withheld in Full as b4 (CCI/TS) immediately following this page

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/s/

RYAN P OWEN
09/20/2012

KIMBERLY L BERGMAN
09/20/2012