

Clinical Pharmacology Review

<u>NDA:</u>	21-928 SDN 1204
<u>Date Received:</u>	8-17-2011
<u>Product Name:</u>	Chantix Tablets
<u>Active Ingredient:</u>	Varenicline Tartarate
<u>Sponsor:</u>	Pfizer Inc.
<u>Type of Submission:</u>	Prior Approval Supplement - Labeling Supplement
<u>Reviewer:</u>	Srikanth C. Nallani, Ph.D.

Background

Pfizer submitted a labeling supplement based on results from a pediatric study conducted to fulfill post-marketing commitment (PMC) # 1.

1. To conduct a study to determine the multiple-dose pharmacokinetics of varenicline in pediatric patients in order to determine the appropriate doses for efficacy and safety evaluations in adolescent smokers, ages 12 through 16, inclusive, to determine the adverse event profile in adolescent patients, and to establish whether there is any age group (or weight group) for whom varenicline is so poorly tolerated that its utility as an aid to smoking cessation treatment should not be evaluated in that group.

The sponsor conducted study A3051070 adequately to address the objectives laid out in the post-marketing commitment #1. Study A3051070 is a "Phase 1, Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Multiple-Dose Pharmacokinetics, Safety and Tolerability of Varenicline in Healthy Adolescent Smokers". The study report was previously reviewed and documented in Darrrts on 2/11/2010. Dr. Hao Zhu also reviewed the PK data from this study report (see review in Darrrts dated 1/29/10). Pfizer has satisfactorily fulfilled Post-Marketing Commitment # 1 for NDA 21-928.

On May 25, 2011 Division of Anesthesia, Analgesia and Addiction Products agreed with the sponsor to revise pediatric pharmacokinetic information based on pediatric study A3051070. The labeling recommendation based on the discussions is as follows:

Section 12.3 Pharmacokinetics (highlighted text added by Pfizer):

Pediatric Patients: Because the safety and effectiveness of CHANTIX in pediatric patients have not been established, CHANTIX is not recommended for use in patients under 18 years of age. [Single and multiple-dose pharmacokinetics of varenicline have been investigated in pediatric patients aged 12 to 17 years old \(inclusive\) and were approximately dose-proportional over the 0.5 mg to 2 mg daily dose range studied. Steady-state systemic exposure in adolescent patients of bodyweight >55 kg, as assessed by AUC \(0-24\), was comparable to that noted for the same doses in the adult population. When 0.5 mg BID was given, steady-state daily exposure of varenicline was, on average, higher \(by approximately 40%\) in adolescent patients with bodyweight < 55 kg compared to that noted in the adult population.](#)

Recommendation: The submitted labeling supplement is acceptable from a clinical pharmacology perspective.

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

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

SRIKANTH C NALLANI
10/05/2011

YUN XU
10/05/2011