

Executive Summary

NDA 21-411, Strattera® (atomoxetine hydrochloride) Pediatric Advisory Committee Meeting 22 March 2006

Patient safety is a top priority at Lilly, and we firmly believe that patients and physicians need to have accurate information to help them make optimal treatment decisions. Thus, Lilly supports the FDA's efforts to remain vigilant in reviewing and evaluating drug utilization and safety. The more a medication is studied and generates information regarding its benefit-risk profile, the more informed healthcare providers and patients can be when making treatment decisions.

Strattera is a safe and effective medication for the treatment of ADHD. Strattera has been extensively studied in clinical trials in more than 5000 children and adolescents with ADHD for up to 5 years, and in almost 1000 adults with ADHD for up to 3 years. Efficacy has been demonstrated in more than 10 registration quality, acute, parallel arm, double-blind, placebo-controlled trials – including separate trials with pediatric patients with ADHD and comorbid tics, depression or anxiety. In addition, atomoxetine (the active ingredient in Strattera) was studied in more than 1000 adults with major depression in the 1980s and early 1990s, although no NDA was ever submitted for this indication due an inability to demonstrate efficacy. However, in the field of ADHD, Lilly believes that Strattera has the most comprehensive drug development and clinical trial database for this indication. Results from Lilly sponsored clinical trials have been presented at multiple scientific meetings, published or submitted for publication, and are further shared via the Lilly clinical trial registry (www.lillytrials.com). Strattera was approved by the FDA in November 2002, and has been used by greater than 3.7 million patients as of February 2006.

As with any medication, the scientific understanding of Strattera broadens as the product continues to be prescribed by practitioners. Postmarketing data are important to collect and evaluate. Lilly works closely with regulatory bodies across the world to monitor, analyze and report post-marketing data and provide timely updates to our product label. Additionally, Lilly is committed to continued research of Strattera in order to provide physicians with the most accurate clinical information and facilitate the discussion of both the benefits and risks of Strattera with their patients or family members.

This briefing package provides information relevant to the focus of this advisory committee meeting. Included are results of two Lilly analyses of the Strattera clinical trial data, as well as the results of three clinical trials in pediatric patients with ADHD and a comorbid condition (tics, major depression, or anxiety). The study with patients with ADHD and tics, was published in *Neurology*. Manuscripts for all of the other analyses or studies are in preparation or have been submitted for publication and are under review.

The enclosed information includes:

- 1) Meta-analysis of Suicide-related Events in Atomoxetine-treated Patients, poster presented at AACAP 2005 (abstract published as Bangs ME, et al. Meta-analysis of suicide-related events in atomoxetine-treated patients. *Scientific Proceedings of the 52nd Annual Meeting of the American Academy of Child & Adolescent Psychiatry*, Toronto, Ont., October 18–23, 2005, Abs. Nr.B49, p. 132).
- 2) Meta-analysis of Aggression or Hostility Events in Atomoxetine Pediatric Trials, poster presented at AACAP 2005 by Polzer J, et al. (abstract published as Tauscher-Wisnie *{sic}* S. Meta-analysis of aggression or hostility events in atomoxetine pediatric trials. *Scientific Proceedings of the 52nd Annual Meeting of the American Academy of Child & Adolescent Psychiatry*, Toronto, Ont., October 18–23, 2005, Abs. Nr. B17, p. 125).
- 3) Atomoxetine Treatment for Pediatric Patients with ADHD and Comorbid Anxiety, poster presented at AACAP 2005 (abstract published as Sumner CJ, et al. Atomoxetine treatment for pediatric patients with ADHD and comorbid anxiety. *Scientific Proceedings of the 52nd Annual Meeting of the American Academy of Child & Adolescent Psychiatry*, Toronto, Ont., October 18–23, 2005, Abs. Nr. B20, p. 125).
- 4) A Study of Atomoxetine in Adolescents with ADHD and Major Depressive Disorder, poster presented at NCDEU 2005 and published online at <http://www.nimh.nih.gov/ncdeu/posterabstracts.cfm> (abstract published as Bangs ME, et al. A study of atomoxetine in adolescents with ADHD and major depressive disorder. *Abstracts: Oral and Poster Presentations*, NCDEU 45th Annual Meeting, Boca Raton, Fla., June 6–9, 2005, p. 187).
- 5) Improvement of ADHD by Atomoxetine in Children with Tic Disorders, poster presented at AACAP 2003 (abstract published as McCracken JT, et al. Improvement of ADHD by atomoxetine in children with tic disorders. *Scientific Proceedings of the 50th Annual Meeting of the American Academy of Child & Adolescent Psychiatry*, Miami Beach, Fla., October 14–19, 2003, Abs. Nr. A35, p. 117).
- 6) Atomoxetine Treatment in Children and Adolescents with ADHD and Comorbid Tic Disorders, manuscript published 27-DEC-2005 (Allen AJ, et al. Atomoxetine treatment in children and adolescents with ADHD and comorbid tic disorders. *Neurology* 2005; 65(12):1941–1949).

Lilly hopes that the committee will find the enclosed information useful as they consider all available evidence related to the important safety deliberations by the FDA and committee members. Clearly benefit and risks have to be assessed collectively. Lilly looks forward to providing further comment on these and other matters during the Advisory Committee hearing on March 22, 2006.