

Briefing Document Addendum

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

Subsequent to the published announcement in the 10 March 2006 Federal Register regarding amendment of the Pediatric Advisory Committee meeting agenda, Lilly is providing an addendum to our briefing document submitted to FDA on 06 March 2006.

This addendum contains the following supplementary attachments relevant to the review and discussion of cardiovascular events at this advisory committee meeting.

Post-marketing Adverse Events

- 7) Limitations in Determining Spontaneous Adverse Event Reporting Rates and Comparing Atomoxetine to other ADHD Medications.

Integrated Analysis of the Atomoxetine Cardiovascular Effect

- 8) Cardiovascular Effects of Atomoxetine in Children, Adolescents, and Adults, manuscript published 2003 (Wernicke, JF et al. Cardiovascular effects of atomoxetine in children, adolescents, and adults. *Drug Safety* 2003; 26(10):729–740).

Evaluation of the Stimulant and Potential Abuse Liability of Atomoxetine

- 9) Atomoxetine Increases Extracellular Levels of Norepinephrine and Dopamine in Prefrontal Cortex of Rat: A Potential Mechanism for Efficacy in Attention Deficit/Hyperactivity Disorder, manuscript published 2002 (Bymaster, FP et al. Atomoxetine increases extracellular levels of norepinephrine and dopamine in prefrontal cortex of rat: a potential mechanism for efficacy in attention deficit/hyperactivity disorder. *Neuropsychopharmacology* 2002; 27(5):699-711).
- 10) Atomoxetine Blocks Motor Hyperactivity in Neonatal 6-Hydroxydopamine-lesioned Rats: Implications for Treatment of Attention-Deficit Hyperactivity Disorder, manuscript published 2005 (Moran-Gates, T et al. Atomoxetine blocks motor hyperactivity in neonatal 6-hydroxydopamine-lesioned rats: implications for treatment of attention-deficit hyperactivity disorder. *International Journal of Neuropsychopharmacology* 2005; 8:439-444).
- 11) Abuse Liability Assessment of Atomoxetine in a Drug-abusing Population, poster presented at CINP 2004 (abstract published as Jasinski DR, et al. Abuse liability assessment of atomoxetine in a drug-abusing population. *Int J Neuropsychopharmacol* 2004; 7(suppl 1): S310. Abs P02.014. 24 June 2004.

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.