PUBLIC SUMMARY DOCUMENT
Product: Atomoxetine hydrochloride, capsules, 80 mg and 100 mg, Strattera®
Sponsor: Eli Lilly Australia Pty Ltd
Date of PBAC Consideration: July 2008

1. Purpose of Application

1) To request an Authority required PBS listing for two new strengths (80 mg and 100 mg) of atomoxetine for the treatment of patients with attention deficit hyperactivity disorder (ADHD);

2) To request a change to the wording of the restriction to include the treatment of adolescents and adults, consistent with the Product Information, and to seek the removal of the requirement for patients to be diagnosed between the ages 6 and 18 years of age.

2. Background

At the November 2006 meeting, the PBAC recommended an authority required listing for initial and continuing treatment of ADHD in patients diagnosed by a paediatrician or psychiatrist between the ages of 6 and 18 years inclusive who meet certain criteria on a cost effectiveness basis over placebo at the new price proposed. The requested restriction was the same as proposed in July 2006 submission. The PBAC accepted that there was a clinical need for this product and that the restriction appropriately targeted those patients most likely to benefit from treatment.

Details of previous submissions are reported in the November 2006 PBAC Public Summary Document "as per sections 5, 6, 7 8.

3. Registration Status

Atomoxetine 80 mg and 100 mg capsules were TGA registered on 22 August 2008 for the 'treatment of Attention Deficit Hyperactivity Disorder (ADHD) as defined by DSM-IV criteria in children 6 years of age and older, adolescents and adults.'

4. Listing Requested and PBAC's View

*Requested changes to the current listing are shown by ~~strikethrough~~ and **bold.***
Authority required

~~Initial treatment of attention-deficit hyperactivity disorder (ADHD) diagnosed between the ages of 6 and 18 years inclusive, by a paediatrician or psychiatrist according to the DSM-IV criteria, where:~~

Initial treatment of attention-deficit hyperactivity disorder (ADHD) diagnosed by a paediatrician or psychiatrist according to the DSM-IV criteria in children 6 years of age and older, adolescents and adults, where:

(a) treatment with dexamphetamine sulfate or methylphenidate hydrochloride poses an unacceptable medical risk due to the following contraindications as specified in the TGA-approved product information:
(1) The patient has a history of substance abuse or misuse (other than alcohol); and/or
(2) The patient has comorbid motor tics or Tourette's Syndrome; and/or
(3) The patient has comorbid severe anxiety diagnosed according to the DSM-IV; or

(b) treatment with dexamphetamine sulfate or methylphenidate hydrochloride has resulted in the development or worsening of a comorbid mood disorder (diagnosed according to the DSM-IV criteria i.e. anxiety disorder, obsessive compulsive disorder, depressive disorder) of a severity necessitating permanent stimulant treatment withdrawal; or where the combination of stimulant treatment with another agent would pose an unacceptable medical risk of a severity necessitating permanent stimulant treatment withdrawal; or

(c) treatment with dexamphetamine sulfate AND methylphenidate hydrochloride has resulted in the development of adverse reactions of a severity necessitating permanent treatment withdrawal:
(1) Adverse effects on growth and weight; and/or
(2) Adverse effects on sleep including insomnia; and/or
(3) Adverse effects on appetite including anorexia.

Authority required

Continuing treatment where the patient has previously been issued with an authority prescription for this drug.

For PBAC's view, see Recommendation and Reasons.

5. Clinical Place for the Proposed Therapy

Reported in the November 2006 PBAC Public Summary Document

6. Comparator

Reported in the November 2006 PBAC Public Summary Document

7. Clinical Trials

Reported in the November 2006 PBAC Public Summary Document

8. Results of Trials

Reported in the November 2006 PBAC Public Summary Document

The submission presented arguments for the addition of two new strengths, which appear in particular to be appropriate for the adolescent and adult market as well for obese children, as follows:

- Atomoxetine is a weight-based dosing regime and that the availability of the 80 mg strength allowed a 67 kg person to be treated with 80 mg once daily instead of 40 mg twice daily. The submission stated that clinical studies included in the registration dossier demonstrate that once daily dosing is as efficacious as twice daily dosing.
- The submission stated that the introduction of the 80 mg and 100 mg strengths would not lead to an increase in the risk of suicidality or other adverse effects.

Estimation of use and costs:
The submission stated that the cost per day is consistent with the costing used in the cost-effectiveness modelling previously accepted by the PBAC, whereby the cost per day per

patient was estimated at 1.3 times the cost per capsule to account for the proportion of patients requiring two or more capsules per day to achieve efficacy.

Additionally, the submission presented arguments for expanding the restriction to allow access to patients over 6 years of age (including adolescents and adults) regardless of when they were diagnosed.

The submission stated that this would allow clinicians to prescribe atomoxetine for adults with ADHD who in the opinion of the clinician, would have had the condition as a child but may not have received the diagnosis as a child.

The submission stated that approximately 60% of those with childhood ADHD will have the disorder continue into adulthood. The diagnosis in an adult is made by establishing a retrospective childhood diagnosis, evaluating the current symptom profile and excluding alternative medical and psychiatric causes of symptoms. These symptoms must have been present in childhood although may not have been recognised.

The submission argued that altering the wording of the restriction to allow patients older than 6 years of age access to PBS-subsidised atomoxetine, no matter when diagnosed, would decrease the administrative requirement (which is currently that doctors make a statement to Medicare Australia that the patient had the condition as a child as outlined above) and that the drug would still be limited to prescribing by specialists.

For PBAC's view, see Recommendation and Reasons.

9. Clinical Claim

Reported in the November 2006 PBAC Public Summary Document

10. Economic Analysis

The submission did not present an economic evaluation.

11. Estimated PBS Usage and Financial Implications

The submission claimed that the additional strengths of atomoxetine were unlikely to increase the number of patients diagnosed or the number of patients prescribed atomoxetine for ADHD and that the cost to the PBS would be neutral, and may result in some modest cost savings to the Government.

The proportion of patients requiring two or more capsules per day in the previous submission was estimated at 30% based on data from the UK and US. The submission stated that since the introduction of the 80 mg and 100 mg strengths in the US in 2007, less than 2% demand is for the 100 mg capsules and 5.3% is for the 80 mg capsules.

The submission stated that alteration of the restriction wording may increase the use of atomoxetine, particularly given the request to include the 80 mg and 100 mg on the PBS, but again stated that the restriction change would reduce the administrative burden and associated costs.

12. Recommendation and Reasons

The PBAC recommended the listing of two new strengths, 80 mg and 100 mg of atomoxetine on the PBS, on the basis of a clinical need for higher strengths in patients with a higher weight. Listing was recommended at the prices proposed in the submission, noting that the maximum quantity of these strengths limits use to one capsule per day.

The PBAC reaffirmed the requirement for diagnosis of attention-deficit hyperactivity disorder (ADHD) between the ages of 6 to 18 years of age, as the clinical and cost effectiveness of treatment with atomoxetine in patients first presenting with ADHD as adults is not known. In light of this, the directive to Medicare Australia from the Department to approve authority applications for patients diagnosed over the age of 18 years where the doctor is prepared to state that, in his/her opinion, the patient would have been diagnosed with ADHD as a child had such a possibility been open to them is to be withdrawn.

The PBAC recommended the NOTE "No applications for increased maximum quantities and/or repeats will be authorised" be applied to all strengths of atomoxetine. The maximum recommended total daily dose in the product information for atomoxetine is 100 mg. The addition to the PBS of the new strengths, 80 mg and 100 mg, of atomoxetine will negate the need for increased maximum quantities of the lower strengths. The PBAC also recommended the addition of the text "sole PBS-subsidised" treatment be added to the atomoxetine restriction, to remind prescribers that the intent of the restriction is for atomoxetine to be prescribed as a single agent for the treatment of ADHD.

Recommendation

ATOMOXETINE HYDROCHLORIDE, capsules, 80 mg and 100 mg.

Restriction:

Authority required

Initial sole PBS-subsidised treatment of attention-deficit hyperactivity disorder (ADHD) diagnosed between the ages of 6 and 18 years inclusive, by a paediatrician or psychiatrist according to the DSM-IV criteria, where:

(a) treatment with dexamphetamine sulfate or methylphenidate hydrochloride poses an unacceptable medical risk due to the following contraindications as specified in the TGA-approved product information:
(1) The patient has a history of substance abuse or misuse (other than alcohol); and/or
(2) The patient has comorbid motor tics or Tourette's Syndrome; and/or
(3) The patient has comorbid severe anxiety diagnosed according to the DSM-IV; or

(b) treatment with dexamphetamine sulfate or methylphenidate hydrochloride has resulted in the development or worsening of a comorbid mood disorder (diagnosed according to the DSM-IV criteria i.e. anxiety disorder, obsessive compulsive disorder, depressive disorder) of a severity necessitating permanent stimulant treatment withdrawal; or where the combination of stimulant treatment with

another agent would pose an unacceptable medical risk of a severity necessitating permanent stimulant treatment withdrawal; or

(c) treatment with dexamphetamine sulfate AND methylphenidate hydrochloride has resulted in the development of adverse reactions of a severity necessitating permanent treatment withdrawal:
(1) Adverse effects on growth and weight; and/or
(2) Adverse effects on sleep including insomnia; and/or
(3) Adverse effects on appetite including anorexia.

Authority required
Continuing sole PBS-subsidised treatment where the patient has previously been issued with an authority prescription for this drug.

NOTE:
No applications for increased maximum quantities and/or repeats will be authorised.

Maximum quantity: 28 (80 mg and 100 mg)
Repeats: 5

13. Context for Decision

The PBAC helps decide whether and, if so, how medicines should be subsidised in Australia. It considers submissions in this context. A PBAC decision not to recommend listing or not to recommend changing a listing does not represent a final PBAC view about the merits of the medicine. A company can resubmit to the PBAC or seek independent review of the PBAC decision.

14. Sponsor's Comment

Eli Lilly welcomes the PBAC's decision to list two additional strengths of atomoxetine on the PBS. However, Eli Lilly is concerned with the inequity in subsidized availability of atomoxetine for adults with ADHD. ADHD is a developmental disorder and it is well documented that access to mental health diagnostic services in Australia is suboptimal, and therefore many adults would not have been able to access diagnostic services as children. Adult patients who are retrospectively diagnosed should be able to access PBS medicines regardless of whether they were able to access diagnostic services as a child, especially if, in the opinion of the prescriber, the patient meets the criteria for diagnosis of ADHD. Currently there are no treatments available on the PBS for patients with ADHD diagnosed after the age of 18 years.