CEDAC FINAL RECOMMENDATION on RECONSIDERATION and REASONS for RECOMMENDATION

MIXED AMPHETAMINE SALTS (Adderall XR® – Shire Canada Inc.)

Description:

Adderall XR® contains dextroamphetamine and levoamphetamine salts in a 3:1 ratio. The Canadian Expert Drug Advisory Committee had previously recommended that Adderall XR not be listed (see Notice of CEDAC Final Recommendation on Adderall XR issued on November 24, 2004). A new indication for use in adolescents and adults and new clinical trial information in children were the basis for the resubmission. Adderall XR is approved for the treatment of Attention Deficit Hyperactivity Disorder (ADHD).

Dosage Forms:

Capsules containing both immediate and extended release pellets of mixed amphetamine salts: 5 mg, 10 mg, 15 mg, 20 mg, 25 mg and 30 mg. The recommended dose ranges from 5 mg to 30 mg, taken once daily.

Recommendation:

The Canadian Expert Drug Advisory Committee (CEDAC) recommends that Adderall XR not be listed.

Reasons for the Recommendation:

1. There is insufficient evidence that Adderall XR offers a therapeutic advantage over less expensive formulations of other stimulant agents such as methylphenidate and dexamphetamine.

2. While Adderall XR has been shown to improve some clinical rating scales in children, adolescents and adults when compared with placebo in short-term (<4 week) trials, no long-term randomized trials have investigated whether this translates into improvement in clinically important outcomes such as quality of life, academic performance and behavioural outcomes.

3. Adderall XR has not been shown to be cost-effective when used as first-line therapy. The Committee considered whether Adderall XR should be listed for patients who had not achieved adequate control of symptoms with a trial of methylphenidate or dexamphetamine. However, there is insufficient evidence from clinical trials that Adderall XR is effective, and therefore cost-effective, in this group of patients. Given the prevalence and importance of ADHD, the Committee felt that it would be important, feasible and ethical to conduct a trial in patients who have failed to respond to methylphenidate or dexamphetamine.

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Summary of Committee Considerations:

The Committee considered two systematic reviews of double blind randomized controlled trials (RCTs) of Adderall XR in the treatment of ADHD, one in adolescents and adults, and one systematic review of trials in children completed subsequent to the review by the Committee in 2004.

Two trials met the inclusion criteria for the systematic review in children, an 18 day trial comparing Adderall XR to atomoxetine in 215 children and a three week placebo controlled cross-over trial in 52 children. Adderall XR improved measures of deportment and attention, and resulted in better performance on a 10-minute math test. A higher proportion of patients treated with Adderall XR were rated as being very much or much improved by clinicians compared to placebo. These results are consistent with those considered by the Committee in 2004. Compared to atomoxetine, another long acting agent for ADHD which is not funded by most drug plans, Adderall XR resulted in significantly greater improvements in measures of deportment and attention, 10-minute math test results, and the proportion of participants rated by clinicians as being very much or much improved. There was no statistically significant difference in changes in quality of life between Adderall XR and atomoxetine.

Two placebo controlled trials of four weeks duration met the inclusion criteria for the systematic review in adolescents and adults, one in each age group. Both trials reported statistically significant improvement with Adderall XR on an ADHD symptom scale (ADHD Rating Scale) and a higher proportion of patients treated with Adderall XR were rated by clinicians as being very much or much improved. There was no statistically significant difference in quality of life in the one trial that measured this outcome.

There were no statistically significant differences between groups in the incidence of serious adverse events in any of the trials. In the trial in adults, there were statistically significantly more withdrawals due to adverse events with Adderall XR compared with placebo. The most common adverse effects of Adderall XR are insomnia, anorexia and weight loss.

Adderall XR costs $2.75 per day, regardless of the dose. This is more costly that methylphenidate immediate release ($0.25 to $0.50 at 20mg to 40mg per day), and similar in cost compared to methylphenidate extended release ($2.09 to $3.38 at 18mg to 54 mg per day) and dextroamphetamine ($0.52 to $6.26 at 5mg to 60mg per day).

Of Note:

1. Both published and unpublished data were reviewed and taken into consideration in making this recommendation.

Background:

CEDAC provides formulary listing recommendations to publicly funded drug plans. Recommendations are based on an evidence-based review of the medication's effectiveness and safety and an assessment of its cost-effectiveness in comparison to other available treatment options. For example, if a new medication is more expensive than other treatments, the Committee considers whether any advantages of the new medication justify the higher price. If the recommendation is not to list a drug, the Committee has concerns regarding the balance between benefit and harm for the medication, and/or concerns about whether the medication provides good value for public drug plans.

The CEDAC Final Recommendation and Reasons for Recommendation neither takes the place of a medical professional providing care to a particular patient nor is it intended to replace professional advice.

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