Methylphenidate extended release

Product:
METHYLPHENIDATE EXTENDED RELEASE (Biphentin®) 10mg, 15mg, 20mg, 30mg, 40mg, 50mg, 60mg extended release capsule

Class of drugs:
Central nervous system stimulant

Indication:
Treatment of Attention Deficit Hyperactivity Disorder (ADHD)

Manufacturer:
Purdue Pharma Inc.

CED Recommendation

The CED recommended that methylphenidate extended release (Biphentin) be funded through the Exceptional Access Program (EAP) according to specific criteria.

Executive Officer Decision

Based on the CED's recommendation and a subsequent listing agreement with the manufacturer that addresses costs and utilization, the Executive Officer decided to fund methylphenidate extended release (Biphentin) on the Ontario Drug Benefit Formulary.

Status

Funding available through Ontario Public Drug Programs on the Ontario Drug Benefit Formulary as General Benefit with therapeutic notes .

Highlights of Recommendation:

- Biphentin is licensed for use in the treatment of Attention Deficit Hyperactivity Disorder for children aged 6 and older, and in adults.
- The Committee reviewed this drug twice, in February 2007, and in February 2008. The Committee noted that Health Canada has identified rare psychiatric effects, including agitation and hallucinations, from all of the drugs in this class.
- **Overall, the Committee noted that the available evidence supports a clinically meaningful improvement with the use of Biphentin to treat ADHD.** However, the Committee noted the available evidence does not support any treatment or compliance advantages of Biphentin over methylphenidate immediate release, and the price premium of Biphentin versus immediate-release methylphenidate was not warranted.
- Therefore, the Committee recommended that Biphentin only be reimbursed through the Exceptional Access Program (EAP), according to specific criteria.

Background:

Attention Deficit Hyperactivity Disorder (ADHD) is a common psychiatric disorder diagnosed in childhood, affecting an estimated 5-12 percent of school-aged children. Approximately 8-10 percent of boys and 3-4 percent of girls under the age of 18 are diagnosed with ADHD. Most of those children – as many as 80 percent – continue to meet the diagnostic criteria for ADHD in adolescence, as do 60 percent of them in adulthood.

ADHD is characterized by inattention and difficulty concentrating, hyperactivity and impulsiveness. In children, it can affect both school performance and socialization with other kids. ADHD may be related to alterations in brain chemistry and other unspecified interactions among certain hormones.

Biphentin is a long-acting formulation that works for up to 12 hours, in comparison to some other formulations of the drug, which must be administered several times a day. Frequent administration often poses a problem for children who need to have their medication given more than once during the day, while at school, in order to benefit.

continued...

Detailed Discussion:

- The Committee reviewed the initial submission from the manufacturer in February 2007, and reviewed a resubmission appealing the Committee's proposed criteria in February 2008.
- Methylphenidate is effective in treating ADHD in children and adults, but one of its limitations is that it lasts only about 2-2.5 hours. That means patients have to take frequent doses to maintain therapeutic levels.
- Controlled or extended-release formulations of methylphenidate, such as Biphentin, may reduce the frequency of daily dosing.
- The manufacturer claims that Biphentin's biphasic release formulation achieves a relatively rapid onset of action and extended coverage, compared to immediate-release (IR) and sustained-release (SR) methylphenidate. Furthermore, Biphentin is available in a capsule formulation, and can be opened and sprinkled on food, which may facilitate medication use and compliance. The Committee noted that these claims have not been proven in randomized controlled trials.
- The Committee also noted that the evidence submitted is based upon randomized controlled trials comparing Biphentin to IR methylphenidate. The trial data supports similar efficacy and side effect profile between these two agents, but there is a lack of good quality, direct comparison studies to assess the relative efficacy and safety of long-acting ADHD medications compared with short-acting agents.
- Although long-acting agents are dosed once daily, there is no evidence that this added convenience translates into improved treatment adherence or other important clinical outcomes.
- Common side-effects include loss of appetite, difficulty sleeping, headaches, or tics. In addition, Health Canada has identified rare psychiatric effects from this class of medications, such as agitation and hallucinations.
- Other rare side-effects include cardiac events. As a class, patients should not use ADHD drugs if they have high blood pressure, heart disease or abnormalities, hardening of the arteries or over-active thyroid glands. Long-acting ADHD medications cost two to three time more than short-acting agents.
- However, the Committee acknowledged the social implications of ADHD and recommended that long-acting ADHD medications be funded in patients who cannot be adequately managed with short-acting treatments. These include patients who do not receive sufficient symptom control or experience side effects from short-acting agents.
- Long-acting treatments can also be considered in situations where there are administrative or societal barriers associated with short-acting products, such as the inability of a child to receive ADHD medications at school or where there is a risk of abuse of short-acting products.
- **Overall, the Committee noted that the available evidence supports a clinically meaningful improvement with the use of Biphentin to treat ADHD.** However, the Committee noted that the available evidence does not support any therapeutic or compliance advantages of Biphentin to immediate release methylphenidate, and the price premium of Biphentin versus immediate release methylphenidate was not warranted. The Committee therefore recommended funding through the EAP.
- Based on a listing agreement that addresses costs and utilization, Biphentin is listed on the Ontario Drug Benefit Formulary with the following therapeutic notes:

Patients ≥ six years of age diagnosed with ADHD according to Diagnostic and Statistical Manual of Mental Disorders (DSM)-IV criteria and where symptoms are not due to other medical conditions which affect concentration, and who require 12-hour continuous coverage due to academic and/or psychosocial needs, and who meet all of the following:

1. The patient demonstrates significant and problematic disruptive behaviour or has problems with inattention that interfere with learning; AND

2. The medication is prescribed by or in consultation with a specialist in pediatric psychiatry, pediatrics or a general practitioner with expertise in ADHD; AND

3. The patient has been tried on methylphenidate immediate release or methylphenidate slow release or Dexedrine IR or Dexedrine Spansules, and has experienced unsatisfactory results due to poor symptom control, side effects, administrative barriers, or societal barriers.

Administrative barriers include:

- *inability of a school to dose the child at lunch;*
- *the school lunch hour does not coincide with the dosing schedule;*
- *poor compliance with noon or afternoon doses;*
- *the patient is unable to swallow tablets.*

Societal barriers include:

- *the patient or patient's caregiver(s) has (have) a history of substance abuse or diversion of listed immediate-release alternatives;*
- *the patient or patient's caregiver(s) is/are at risk of substance abuse or diversion of listed immediate-release alternatives.*

CEDAC Recommendation:

(http://www.cadth.ca/index.php/en/cdr/recommendations)

The Canadian Expert Drug Advisory Committee (CEDAC) did not review methylphenidate extended release (Biphentin).

Ontario
Ministry of
Health and Long-Term Care
Ontario Public Drug Programs

For more information, please contact:

Ministry of Health and Long-Term Care
Ontario Public Drug Programs
Hepburn Block, 9th Floor
80 Grosvenor Street, Queen's Park
Toronto, Ontario M7A 1R3
or click: http://www.health.gov.on.ca/english/providers/program/drugs/ced_rec_table.html