

Duloxetine (for diabetic peripheral neuropathic pain)

Product:

DULOXETINE (Cymbalta®)
30mg, 60mg capsules

Class of drugs:

Serotonin and norepinephrine reuptake inhibitor (SNRI)

Indication:

Treatment of diabetic peripheral neuropathic pain

Manufacturer:

Eli Lilly Canada Inc.

CED Recommendation

The CED recommended that duloxetine (Cymbalta®) be funded for the treatment of diabetic peripheral neuropathic pain through the Exceptional Access Program according to specific criteria. The CED noted that duloxetine (Cymbalta®) has been shown to reduce pain and improve quality of life in the treatment of diabetic peripheral neuropathic pain. However, there is no evidence that duloxetine (Cymbalta®) is as or more effective than lower cost alternatives.

Executive Officer Decision

Taking into consideration the CED's recommendation, the Executive Officer decided to list duloxetine (Cymbalta®) on the ODB Formulary as a General Benefit, based on a listing agreement with the manufacturer that addresses cost and appropriate utilization.

Status

Funding available through the Ontario Public Drug Programs as a General Benefit on the ODB Formulary.

Highlights of Recommendation:

- ◆ Duloxetine is indicated for the treatment of diabetic peripheral neuropathic pain (nerve pain in the arms and legs experienced by some patients with diabetes) as well as for the treatment of depression. This review is specific to its use in the management of neuropathic pain in patients with diabetes.
- ◆ The Committee evaluated three studies comparing the effects of duloxetine to placebo in adult patients with diabetic peripheral neuropathic pain. Compared with placebo, patients treated with duloxetine reported reductions in pain and improvements in their quality of life.
- ◆ There are no comparison studies between duloxetine and other treatments for diabetic peripheral neuropathic pain; therefore, its efficacy relative to alternative therapies is unknown.
- ◆ Available studies for duloxetine in the treatment of diabetic peripheral neuropathic pain were short in duration (12 weeks). The long-term safety of this drug is uncertain.
- ◆ Common side effects reported with duloxetine include nausea, dizziness, fatigue and sleepiness.
- ◆ At the recommended dose of 60mg daily, duloxetine costs \$3.56 per day. It is more expensive than alternative treatments such as amitriptyline, carbamazepine, and opioid analgesics that are listed on the Formulary. Duloxetine is similar in cost to gabapentin, a neuropathic pain treatment funded through the Exceptional Access Program.
- ◆ **Overall, the Committee acknowledged that duloxetine has been shown to reduce pain and improve quality of life in the treatment of diabetic peripheral neuropathic pain compared with placebo. However, there is no evidence that duloxetine is as or more effective than lower cost alternatives listed on the formulary. Furthermore, the**

long-term safety of this drug has not been established. In consideration of the difficult-to-treat nature of neuropathic pain, the Committee recommended that funding be considered through the Exceptional Access Program according to specific criteria.

Background:

Diabetic neuropathy is a nerve disorder caused by poor blood sugar control in patients with diabetes. Diabetic peripheral neuropathy is the most common type of diabetic neuropathy. Symptoms of diabetic peripheral neuropathy include pain, numbness and tingling in the toes, feet, legs, hands, and arms.

The goal of treating diabetic peripheral neuropathy is to primarily relieve discomfort. The first step is to bring blood sugar levels under control. Drug treatments may be prescribed for the relief of pain, burning, or tingling. Analgesics, antidepressants, and anticonvulsant medications are commonly used for the management of diabetic peripheral neuropathic pain. Many of these treatments are listed on the ODB Formulary. Funding for other therapies, such as gabapentin and pregabalin, are considered through the Exceptional Access Program.

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Detailed Discussion:

- ◆ The Committee reviewed three double-blind randomized controlled studies evaluating the efficacy and safety of duloxetine for diabetic peripheral neuropathic pain. The studies were 12 weeks in duration and compared duloxetine with placebo in a total of 1,139 patients.
- ◆ The studies reported that duloxetine, at doses of 60mg daily and 60mg twice daily, was effective in reducing pain, as measured by a reduction in 24-hour average pain scores. Improvements in quality of life measures were also observed in patients who were treated with duloxetine compared with placebo.
- ◆ Duloxetine 60mg twice daily was not shown to be significantly better in pain control than the 60mg once daily dose, and the 60mg twice daily dose was associated with more adverse events.
- ◆ Because direct comparison studies between duloxetine and alternative neuropathic pain treatments are not available, its efficacy versus other agents is unknown.
- ◆ There are no randomized controlled studies evaluating the long-term safety of duloxetine. Given that diabetic peripheral neuropathic pain is a chronic condition, the Committee was concerned about the lack of long-term safety data. It was noted that the Food and Drug Administration in the United States recently updated warnings on the risk of hyponatremia (low blood sodium levels), bleeding, and urinary hesitancy/retention associated with the use of duloxetine.
- ◆ At the recommended dose of 60mg daily, duloxetine costs \$3.56 per day. It is more expensive than alternative treatments such as amitriptyline, carbamazepine, and opioid analgesics that are listed on the Formulary. Duloxetine is similar in cost to gabapentin, which is funded through the Exceptional Access Program.
- ◆ The Committee acknowledged that diabetic peripheral neuropathic pain may sometimes be difficult to treat and that having more treatment options would be valuable in patients who do not respond to standard therapies.
- ◆ Overall, the Committee noted that duloxetine has been shown to reduce pain and improve quality of life in the treatment of diabetic peripheral neuropathic pain compared with placebo.

However, there is no evidence that duloxetine is more effective than lower cost alternatives listed on the Formulary. Furthermore, the long-term safety of this drug has not been established.

CEDAC Recommendation:

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

The Canadian Expert Drug Advisory Committee (CEDAC) recommended that duloxetine (Cymbalta®) be listed for the treatment of neuropathic pain in diabetic patients according to criteria.



Ministry of
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