Drug Coverage Decision for B.C. PharmaCare

About PharmaCare B.C. PharmaCare is a government-funded drug plan. It helps British Columbians with the cost of eligible prescription drugs and specific medical supplies.

Details of Drug Reviewed

Drug	**levodopa-carbidopa**
Brand Name	**Duodopa®**
Dosage Form(s)	20 mg / mL levodopa and 5 mg / mL carbidopa monohydrate intestinal gel
Manufacturer	AbbVie Corporation
Submission Type	**Resubmission**
Use Reviewed	advanced Parkinson's disease
Common Drug Review (CDR)	Yes, CDR recommended: **to Reimburse with clinical criteria and/or conditions**. Visit the CDR website for more details: https://www.cadth.ca/sites/default/files/cdr/complete/SR0557_Duodopa_Aug_24-18.pdf
Drug Benefit Council (DBC)	DBC met on October 1, 2018. DBC considered various inputs including: clinical and pharmacoeconomic evidence review material and the recommendations from the Canadian Drug Expert Committee (CDEC). The DBC also considered Patient Input Questionnaire responses from 37 patients, 17 caregivers, and one Patient Group, patient input provided to the CDR, an Other Drug Agencies Review Recommendations document, and a Budget Impact Assessment.
Drug Coverage Decision	**Limited Coverage.** Access the levodopa-carbidopa criteria from: **www.gov.bc.ca/pharmacarespecialauthority**
Date	December 10, 2020
Reason(s)	**Drug coverage decision is inconsistent with the DBC recommendation.** • In report "Deep brain stimulation or Duodopa for advanced Parkinson's disease in British Columbia", published by BC Health Technology Review Office, deep brain stimulation (DBS) was advantageous to the treatment with Duodopa. However, patients in British Columbia still experience long wait times to access DBS procedure and in selected patients Duodopa could be used in the meantime. • Duodopa demonstrated advantage in reduction in patients' "off" time at week 12 compared with immediate-release oral levodopa-carbidopa therapy. • Coverage of Duodopa may be reassessed once DBS becomes more accessible.
Other Information	None

The Drug Review Process in B.C.

A manufacturer submits a request to the Ministry of Health (Ministry).

An independent group called the Drug Benefit Council (DBC) gives advice to the Ministry. The DBC looks at:

- whether the drug is safe and effective
- advice from a national group called the Common Drug Review (CDR)
- what the drug costs and whether it is a good value for the people of B.C.
- ethical considerations involved with covering or not covering the drug
- input from physicians, patients, caregivers, patient groups and drug submission sponsors

The Ministry makes PharmaCare coverage decisions by taking into account:

- the existing PharmaCare policies, programs and resources
- the evidence-informed advice of the DBC
- the drugs already covered by PharmaCare that are used to treat similar medical conditions
- the overall cost of covering the drug

Visit the The Drug Review Process in B.C. - Overview and Ministry of Health - PharmaCare for more information.

This document is intended for information only.
It does not take the place of advice from a physician or other qualified health care provider.

Drug Benefit Council (DBC) Recommendation and Reasons for Recommendation

FINAL

Levodopa-carbidopa intestinal gel (Duodopa®)

AbbVie Corporation

Description:

Drug review of **levodopa-carbidopa intestinal gel (Duodopa®)** for the following Health Canada approved indications:

For the treatment of patients with advanced levodopa-responsive Parkinson's disease (PD).

In their review, the DBC considered the following: the final reviews completed by the Common Drug Review (CDR) on August 22, 2018, which included clinical and pharmacoeconomic evidence review material and the recommendations from the Canadian Drug Expert Committee (CDEC). The DBC also considered Patient Input Questionnaire responses from 37 patients, 17 caregivers, and one Patient Group, patient input provided to the CDR, an Other Drug Agencies Review Recommendations document, and a Budget Impact Assessment.

Dosage Forms:

Duodopa® is available as 20 mg/mL levodopa and 5 mg/mL carbidopa gel for intestinal infusion.

Recommendations:

1. The Drug Benefit Council (DBC) recommends that levodopa-carbidopa intestinal gel (Duodopa®) not be listed.

Of Note:

- DuoDopa may be considered for coverage in extraordinary cases in patients who do not have access to direct brain stimulation (DBS).

Reasons for the Recommendation:

1. Summary

- There is a lack of evidence directly comparing levodopa-carbidopa intestinal gel with DBS, which is the preferred treatment and standard of care in patients with advanced Parkinson`s disease who no longer have a good response to oral therapy or who have unacceptable motor fluctuations.
- At the manufacturer's submitted price, the annual cost of DuoDopa is many times higher than the annual cost of all other comparable treatment options for advanced Parkinson's disease, including other levodopa-carbidopa products, and is also significantly higher than the estimated cost of DBS.

2. Clinical Efficacy

- The DBC considered the CDR systematic review, which included one new phase III, double-blind, double-dummy, multi-centre, superiority randomized controlled trial (RCT) designed to assess the benefits and harms of levodopa-carbidopa intestinal gel compared to immediate-release oral levodopa-carbidopa (Study 001/002), and one non-comparative, multi-national, multicenter, open-label, long-term safety study (Study 004).
- Study 001/002 demonstrated that levodopa-carbidopa intestinal gel was associated with a statistically significant and clinically meaningful reduction in patients' "off" time at week 12 compared with immediate-release oral levodopa-carbidopa capsules, and with significant improvement in the amount of "on" time without troublesome dyskinesia at week 12.
- The Unified Parkinson's Disease Rating Scale (UPDRS), Part II and Parkinson disease questionnaire (PDQ-39) Summary Index Score showed statistically significant and clinically meaningful improvements in Parkinson`s disease symptoms in favour of levodopa-carbidopa intestinal gel at week 12.
- There was no clinical trial evidence available comparing levodopa-carbidopa intestinal gel with DBS (DBS).
- For detailed information on the systematic review of levodopa-carbidopa intestinal gel (Duodopa), please see the CDEC Final Recommendation at: https://www.cadth.ca/levodopa-carbidopa-drug-plan-submission.

3. Safety

- One non-comparative, open-label, multi-centre, long-term safety study (Study 004) designed to assess the safety of levodopa-carbidopa intestinal gel over 54 weeks demonstrated that levodopa-carbidopa intestinal gel use was not associated with important harms.
- For detailed information on the safety and tolerability of levodopa-carbidopa intestinal gel (Duodopa), please see the CDEC Final Recommendation at the link above.

4. Economic Considerations

- At the manufacturer's submitted price, the annual cost of treatment with DuoDopa was from 12 and 120 times higher than the annual cost of other comparable treatment options for advanced Parkinson's disease, including other levodopa-carbidopa products, and is also significantly higher than the estimated cost of DBS.

- The manufacturer's submitted price did not include the additional treatment costs associated with DuoDopa that need to be considered, including the cost of endoscopic insertion of the PEG-J tube, and the health care system resources required for this procedure and for subsequent maintenance.
- There is a high risk of wastage with levodopa-carbidopa intestinal gel, as once a cassette is taken out of the refrigerator it must be used within 16 hours or discarded. According to the CDR, in the majority of patients, approximately half of the cassette would be discarded.

5. Of Note

- DBS is the preferred treatment and standard of care for patients with advanced Parkinson`s disease who no longer have a good response to oral therapy or who have unacceptable motor fluctuations. However, DBS requires access to neurosurgical resources that may be limited, and the procedure may be contraindicated in some patients.
- The DBC considered Patient Input Questionnaire responses from 37 patients, 17 caregivers, and one Patient Group. Patients who had tried DuoDopa indicated that the continual dosing reduced the unpredictability of Parkinson`s symptoms and reduced the frequency of "off" periods experienced with timed oral formulations.