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CADTH Reimbursement Recommendation

Foslevodopa-Foscarbidopa (Vyalev)

Indication: For the treatment of motor fluctuations in patients with advanced levodopa-responsive Parkinson's disease who do not have satisfactory control of severe, debilitating motor fluctuations and hyper-/dyskinesia despite optimized treatment with available combinations of Parkinson's medicinal products

Sponsor: AbbVie Corporation

Final recommendation: Reimburse with conditions

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Summary

What Is the CADTH Reimbursement Recommendation for Vyalev?

CADTH recommends that Vyalev should be reimbursed by public drug plans for the treatment of motor fluctuations in patients with advanced levodopa-responsive Parkinson disease (PD) who do not have satisfactory control of severe, debilitating motor fluctuations and hyperkinesia or dyskinesia despite optimized treatment with available combinations of medicinal products for PD if certain conditions are met.

Which Patients Are Eligible for Coverage?

Vyalev should only be covered to treat patients with advanced PD who have unpredictable changes in movement symptoms and severe limitations in being able to perform daily activities while receiving optimized oral therapy. Patients should have previously shown improvement in their symptoms when they received levodopa treatment and should not have severe psychosis or severe dementia. Patients or caregivers should be able to understand how to use the drug infusion system correctly.

What Are the Conditions for Reimbursement?

Vyalev should only be reimbursed if prescribed by neurologists who are specialized in managing movement disorders or with expertise in managing advanced PD. Its cost should not be more than other treatments that are reimbursed for the treatment of advanced PD. Vyalev may lead to more patients seeking treatment; this adds uncertainty in the budget impact which should be addressed.

Why Did CADTH Make This Recommendation?

- Evidence from a clinical trial demonstrated that Vyalev reduced unpredictable changes in movement symptoms in patients with advanced PD whose movement symptoms were uncontrolled with oral therapy.
- Vyalev treatment may meet needs identified by patients as important, including reducing fluctuations of motor symptoms and pill burden and by providing a nonsurgical treatment option.
- Based on CADTH's assessment of the health economic evidence, uncertainty remains about whether Vyalev represents good value to the health care system at public list prices. A price reduction may be required.
- Based on public list prices, Vyalev is estimated to have no additional cost to public drug plans over the next 3 years. However, Vyalev

Summary

may increase public drug plan budgets if its availability results in patients who were not previously on treatment to seek access to Vyalev and/or if Vyalev displaces deep brain stimulation.

Additional Information

What Is Advanced PD?

PD is a condition in which the brain cells responsible for controlling movement become damaged or die, leading to symptoms such as tremor, stiffness, slow movement, and difficulty with balance and coordination. Advanced PD refers to the later stages of the condition when symptoms become more severe and challenging to manage. It is estimated that more than 100,000 people living in Canada are diagnosed with PD, and approximately 10% to 20% of them with advanced PD.

Unmet Needs in Advanced PD

Existing treatments for advanced PD (e.g., deep brain stimulation and levodopa-carbidopa intestinal gel) could be difficult to access for some patients because these are typically provided in major urban treatment centres. These treatments can cause surgical complications and are not suitable for some patients due to side effects and other individual factors that would make the treatment unsafe.

How Much Does Vyalev Cost?

Treatment with Vyalev is expected to have an annual cost of $62,023 per patient assuming patients will use approximately 1 vial per day.

Recommendation

The CADTH Canadian Drug Expert Committee (CDEC) recommends that foslevodopa-foscarbidopa be reimbursed for the treatment of motor fluctuations in patients with advanced levodopa-responsive Parkinson disease (PD) who do not have satisfactory control of severe, debilitating motor fluctuations and hyperkinesia or dyskinesia despite optimized treatment with available combinations of medicinal products for PD only if the conditions listed in Table 1 are met.

Rationale for the Recommendation

One phase III, double-blind, double-dummy, randomized controlled trial (RCT) (M15-736) demonstrated that treatment with foslevodopa-foscarbidopa resulted in statistically significant and clinically meaningful improvements in change in average daily normalized "on" time without troublesome dyskinesia and average daily normalized "off" time from baseline at week 12 compared with oral levodopa-carbidopa (LD-CD) therapy for levodopa-responsive patients with advanced PD who had motor fluctuations inadequately controlled by oral therapy. The mean difference in change in average daily normalized on time without troublesome dyskinesia from baseline to week 12 was 1.75 hours (95% confidence interval [CI], 0.46 hours to 3.05 hours; P = 0.0083), and the mean difference change in average daily normalized off time from baseline to week 12 was −1.79 hours (95% CI, −3.03 hours to −0.54 hours; P = 0.0054).

Patients expressed a need for treatment options that can eliminate motor fluctuations, do not increase dyskinesia over time, treat cognitive issues, reduce pill burden, and reduce sleep interruptions. CDEC concluded that foslevodopa-foscarbidopa met some of the needs identified by patients in terms of reducing motor fluctuations and pill burden. CDEC noted that patient groups indicated a reluctance toward surgical approaches for the treatment of advanced PD, which include deep brain stimulation (DBS) and levodopa-carbidopa intestinal gel (LCIG). Some patients were also interested in subcutaneous approaches, which is the mode that foslevodopa-foscarbidopa is administered.

At the sponsor-submitted price for foslevodopa-foscarbidopa and the publicly listed price for LCIG, foslevodopa-foscarbidopa was cost neutral compared with LCIG when accounting for drug costs only. However, because the sponsor did not provide an economic evaluation comparing foslevodopa-foscarbidopa with other relevant comparators, it is unclear whether a price reduction would be required and the magnitude of this price reduction for foslevodopa-foscarbidopa to achieve an incremental cost-effectiveness ratio of $50,000 per QALY gained.

Table 1: Reimbursement Conditions and Reasons

Reimbursement condition	Reason	Implementation guidance
Initiation		
1. In patients with advanced levodopa-responsive PD only if all of the following criteria are met:	The M15-736 trial demonstrated that foslevodopa-foscarbidopa had clinical benefit in patients diagnosed with	—

Reimbursement condition	Reason	Implementation guidance
1.1. have not been able to achieve satisfactory control of severe, debilitating motor fluctuations and hyperkinesia or dyskinesia despite optimized treatment with available combinations of PD treatments, including maximally tolerated doses of levodopa in combination with carbidopa, a COMT inhibitor, a dopamine agonist, a MAO-B inhibitor, and amantadine, if not contraindicated 1.2. have severe disability associated with at least 25% of the waking day in the off state and/or ongoing, bothersome levodopa-induced dyskinesias, despite having tried frequent dosing of levodopa (at least 5 doses per day) 1.3. have received an adequate trial of maximally tolerated doses of levodopa, with previously demonstrated clinical response 1.4. the patient does not have severe psychosis or severe dementia 1.5. patient or caregiver are able to demonstrate correct understanding and use of the delivery system.	levodopa-responsive advanced PD, taking PD medications at a total daily dose of ≥ 400 mg/day levodopa equivalents, had motor fluctuations and motor symptoms inadequately controlled by current therapy, and had normal cognitive function (MMSE ≥ 24).	
Renewal		
2. Eligibility for foslevodopa-foscarbidopa should be based on the criteria used by each of the public drug plans for the renewal of LCIG in patients with advanced PD.	There was no evidence identified that suggested treatment response to foslevodopa-foscarbidopa would be evaluated differently than treatment response to LCIG.	The patient should continue to benefit from treatment for renewal of foslevodopa-foscarbidopa reimbursement. It is expected that clinicians will continue to monitor their patients and discontinue foslevodopa-foscarbidopa if the patient is no longer benefiting from treatment.
Prescribing		
3. Foslevodopa-foscarbidopa should be prescribed by neurologists who are movement disorder subspecialists or who have expertise in managing advanced PD.	To ensure foslevodopa-foscarbidopa is prescribed only for appropriate patients and managed in an optimized manner.	—

Reimbursement condition	Reason	Implementation guidance
Pricing		
4. A reduction in price.	Because the sponsor did not provide a cost-effectiveness analysis of foslevodopa-foscarbidopa vs. all relevant comparators, the cost-effectiveness of foslevodopa-foscarbidopa is unknown in patients with PD whose disease is not adequately controlled on optimized therapies. A price reduction may be required, although the magnitude of the price reduction remains unknown.	—
Feasibility of adoption		
5. The feasibility of adoption of foslevodopa-foscarbidopa must be addressed.	The magnitude of uncertainty in the budget impact must be addressed to ensure the feasibility of adoption. The availability of foslevodopa-foscarbidopa may result in an increase in patients who were not previously on treatment seeking access to foslevodopa-foscarbidopa which may displace market shares from DBS. The budget impact is expected to increase, although the expected magnitude is unknown.	The sponsor noted within their submission that the infusion pump and its ancillaries to administer foslevodopa-foscarbidopa will be provided by them at no additional costs to public drug plans.

CDEC = CADTH Canadian Drug Expert Committee; COMT = catechol-O-methyltransferase; DBS = deep brain simulation; LCIG = levodopa-carbidopa intestinal gel; MAO-B = monoamine oxidase B; MMSE = Mini-Mental State Examination; PD = Parkinson disease; PEG-J = percutaneous endoscopic gastro-jejunal.

Discussion Points

- Patients expressed a need for treatment options that can eliminate sleep interruptions, treat cognitive issues, and do not increase dyskinesia over time. The M15-736 trial suggested that foslevodopa-foscarbidopa could improve sleep symptoms compared with oral LD-CD therapy, although the results were associated with uncertainty because they were tested after failure of the statistical hierarchy. CDEC noted that no conclusion could be drawn on the relative effect of foslevodopa-foscarbidopa compared with oral LD-CD therapy on cognition because cognition was not an efficacy end point in the M15-736 trial. CDEC also considered evidence from M15-741, which was a phase III, single-arm trial of foslevodopa-foscarbidopa. Results from this trial suggested that foslevodopa-foscarbidopa could maintain on time without troublesome dyskinesia through 52 weeks. However, due to the open-label study design and the lack of comparator and statistical testing, CDEC was unable to conclude that foslevodopa-foscarbidopa could prevent an increase in dyskinesia in the long term.
- CDEC examined evidence from 1 indirect treatment comparison: a network meta-analysis (NMA) submitted by the sponsor assessing the comparative efficacy of foslevodopa-foscarbidopa versus LCIG for the treatment of patients with advanced PD. The study showed that foslevodopa-foscarbidopa was associated with an improvement in sleep symptoms and no difference in on time without troublesome dyskinesia duration and off time duration compared with LCIG; however, there is

uncertainty in the estimated treatment effects due to limitations of the NMA, including heterogeneity of study design and population and a sparse linear network. Therefore, CDEC was unable to determine the relative efficacy of foslevodopa-foscarbidopa compared with LCIG.

- CDEC noted that the safety profile of foslevodopa-foscarbidopa was generally similar to oral LD-CD therapy, except that infusion site reactions and infections were more frequent with foslevodopa-foscarbidopa; most were nonserious, but some led to treatment discontinuation. As well, there is a higher frequency of hallucination or psychosis with foslevodopa-foscarbidopa compared with oral LD-CD therapy, although the clinical expert noted that the risk could be mitigated by careful selection of treatment candidates and conservative dosing.
- CDEC discussed the place in therapy of foslevodopa-foscarbidopa and the appropriateness of considering DBS a relevant comparator. CDEC considered the clinical expert's input that both DBS and LCIG are available for patients who do not have satisfactory control of motor fluctuations despite optimized therapy but acknowledged that there is an unmet need for treatments that require fewer specialists to administer and are not associated with surgical complications. Not all patients will be able to receive DBS or LCIG due to contraindications and adverse effects, and accessing LCIG and DBS may be difficult for patients living in rural or remote areas because these treatments are typically only provided in major urban centres. The clinical expert indicated that foslevodopa-foscarbidopa could potentially require fewer specialist clinicians to initiate and maintain, and administration could improve access.
- A structural assumption within the submitted budget impact analysis was that foslevodopa-foscarbidopa will only displace LCIG. As such, the sponsor did not attempt to identify the costs of DBS or other relevant comparators. CDEC noted that this assumption could not be explored by CADTH. CDEC further discussed that the availability of foslevodopa-foscarbidopa may result in an increased budget impact because patients with advanced PD who have not previously sought treatment and those who would be candidates for invasive treatments (DBS or LCIG) may opt for this therapy. It is expected that reimbursing foslevodopa-foscarbidopa for the treatment of patients with PD whose symptoms not adequately controlled on optimized therapies will increase the budget impact of public drug plans although the expected magnitude is unknown.

Background

PD is the most common movement disorder, with estimated age-standardized incidence rates ranging from 108 per 100,000 to 212 per 100,000 among people aged 65 and older in North America. PD is characterized by motor symptoms, such as bradykinesia, tremor, rigidity, and postural instability, as well as nonmotor symptoms, including cognitive impairment, mood disorders, and sleep problems. Approximately 10% to 20% of patients with PD have advanced disease (i.e., do not achieve satisfactory control of their disease despite optimized oral treatment). Patients with advanced PD may continue to rely on optimization of oral therapy or receive advanced device-aided therapies, including DBS and LCIG, to control motor fluctuations. Optimization of oral therapy could increase the burden and complexity of medication use. DBS and LCIG are invasive

treatments that require a specialized medical team. DBS treatment is also only provided at specialized centres to select patients without contraindications.

Foslevodopa-foscarbidopa has been approved by Health Canada for the treatment of motor fluctuations in patients with advanced levodopa-responsive PD who do not have satisfactory control of severe, debilitating motor fluctuations and hyperkinesia or dyskinesia despite optimized treatment with available combinations of medicinal products for PD. Foslevodopa-foscarbidopa is a prodrug combination of levodopa and carbidopa. It is available as a solution containing 240 mg/mL foslevodopa and 12 mg/mL foscarbidopa for subcutaneous infusion. The product monograph recommends that foslevodopa-foscarbidopa be administered as a continuous subcutaneous infusion, 24 hours per day, using an infusion pump based on an individualized dosing with the dose adjusted for optimal clinical response.

Sources of Information Used by the Committee

To make its recommendation, the committee considered the following information:

- a review of 1 phase III RCT; 1 phase III, single-arm trial; 2 long-term extension studies; and 1 sponsor-provided indirect treatment comparison in patients with advanced PD
- patients' perspectives gathered by patient groups, Parkinson Association of Alberta, Parkinson Canada, Parkinson Society British Columbia, and Parkinson Québec
- input from public drug plans that participate in the CADTH review process
- 1 clinical specialist with expertise diagnosing and treating patients with advanced PD
- input from 2 clinician groups, including the National Movement Disorder Expert Group and the BC Movement Disorders Specialist Group
- a review of the pharmacoeconomic model and report submitted by the sponsor.

Stakeholder Perspectives

The information in this section is a summary of input provided by the patient and clinician groups who responded to CADTH's call for input and from clinical expert(s) consulted by CADTH for the purpose of this review.

Patient Input

CADTH received 1 input from Parkinson Association of Alberta and 1 joint input from Parkinson Canada, Parkinson Society British Columbia, and Parkinson Quebec. Parkinson Association of Alberta conducted a survey of 26 patients with PD and care partners or family in Alberta. The joint input from Parkinson Canada, Parkinson Society British Columbia, and Parkinson Québec gathered responses from 113 patients with PD and caregivers of patients with PD in Canada via a survey; the majority of respondents were from Ontario (72.6%).

According to both inputs, off periods and motor fluctuations associated with PD substantially impacted quality of life and activities of daily living for patients, led to work absenteeism (and some resulted in early retirement), and caused emotional and financial burden to the caregivers. Respondents from both inputs noted that symptoms that are most important to control were changes in cognition and memory, fatigue and sleep issues, freezing and unpredictable off periods, changes in mood, rigidity, speech and swallowing issues, bladder and bowel issues, impaired balance, slowness, and tremors.

Patients were reported to be taking oral medications and more than half experienced side effects, with fatigue, drowsiness, constipation, and bowel issues being most difficult to endure. More than half of the respondents to the joint input reported that high pill burden (up to 40 pills per day) impacted their lifestyle or quality of life. Difficulties related to medication adherence included difficulty with timing or remembering, swallowing, storage of medications, and limited improvement of symptoms. Some patients also included some form of rehabilitation (physiotherapy, occupational and/or speech therapy, or exercise) as a treatment option, but respondents also cited cost, lack of motivation, or lack of access as barriers, especially for patients in rural areas. No respondent from either patient input had received foslevodopa-foscarbidopa at the time of survey.

Respondents indicated the most important unmet needs were treatment options that would not increase dyskinesia as time went on, medications that would treat cognitive issues, and longer-lasting medications that would reduce pill burden and off periods, eliminating the fluctuations and sleep interruptions caused by medications wearing off. The joint input indicated that a large proportion of patients were very reluctant about invasive treatment options, such as DBS or LCIG, and most patients (65%) would be interested in an injection-based levodopa-carbidopa treatment; however, only 1 (3.8%) respondent from Parkinson Association of Alberta said they would consider it and 2 (7.7%) respondents from this group were unsure.

Clinician Input

Input From Clinical Experts Consulted by CADTH

The clinical expert noted there is an unmet need for treatment options that have less resource requirements so that treatment is accessible to patients, especially those residing in rural and remote areas, and does not require the need to travel to major urban centres; as well as treatment options for patients who are ineligible for existing advanced therapies due to the presence of comorbidities. The clinical expert noted that foslevodopa-foscarbidopa could serve as a treatment option in patients with advanced PD and could fill a treatment gap for patients who cannot travel to access other advanced therapies or for patients with comorbidities or a strong personal aversion to other options.

The clinical expert noted that patients with levodopa-responsive advanced PD would be considered eligible for foslevodopa-foscarbidopa treatment in clinical settings. The clinical expert noted there is currently no universally agreed-upon definition for advanced PD, and it would be appropriate to define advanced PD based on the Delphi-based consensus criteria or the “5-2-1” criteria or as “patients with PD who have motor fluctuations inadequately controlled by optimized oral therapy.” Patients with excessive off time or on time with bothersome dyskinesia are more likely to benefit from treatment according to the clinical expert. The

clinical expert noted that patients with levodopa-unresponsive symptoms are not expected to benefit from it because the therapy is a system of delivery for dopamine precursor treatment. The clinical expert noted that a clinically meaningful response would include improvement in on time and off time measurements and quality of life, which would typically be observed at 3 months after initiation. According to the clinical expert, clinical meaningfulness can be judged differently by treating neurologists and by patients, such as the predictability of therapy or the flexibility patients have with longer continuous on periods; as such, a meaningful response may be best left to the discretion of the treating neurologist. The clinical expert noted that treatment discontinuation could be considered when patients experience intolerable adverse events (AEs) or significant functional impairments that are not relieved by the treatment. The drug should be prescribed by neurologists who have experience in the treatment of patients with PD and are trained in the use of this drug, as per the clinical expert.

Clinician Group Input

Input was received from the National Movement Disorder Expert Group, including 11 clinicians, and the BC Movement Disorders Specialist Group, including 7 additional clinicians. Both clinician group inputs were generally aligned with the clinical expert consulted by CADTH.

The inputs concurred regarding unmet needs of patients with advanced PD. Patients receiving oral levodopa have inadequate control of motor fluctuations despite increased dosing frequency over time, and they may have contraindications, poor tolerance, or insufficient response to adjunct medications. The inputs described barriers to access of advanced therapies for PD (i.e., DBS and LCIG treatments) that vary geographically because of limited specialists, uneven distribution of resources geographically, intense resource needs, medical contraindications, poor acceptance from patients due to the invasive nature and risks of the treatments, and the impact of PD itself on patients' ability to travel long distances for DBS or LCIG treatment and to manage at-home aspects of LCIG treatment. Additionally, the inputs noted that there are no current treatments that address the underlying disease process of PD.

The clinician group inputs were aligned that foslevodopa-foscarbidopa could serve as an additional treatment option for patients with advanced PD and could benefit patients experiencing bothersome end-of-dose off periods, unpredictable efficacy of oral therapies due to absorption delays, and/or excessively complex oral medication schedules because foslevodopa-foscarbidopa is delivered subcutaneously.

The clinician groups indicated that, similar to other existing advanced therapies, eligible patients would include those who have levodopa-responsive PD with bothersome motor and nonmotor fluctuations despite optimized oral therapies. The inputs suggested that eligible patients have advanced PD identified by the 5-2-1 criteria. The inputs also suggested that it would be reasonable to recommend having tried at least 1 monoamine oxidase B inhibitor and a catechol-O-methyltransferase inhibitor, unless contraindicated. In patients without cognitive impairment who are younger than 70 years, the inputs also stated it would be reasonable to recommend having tried at least 1 dopamine agonist and amantadine (if dyskinesia is bothersome), unless contraindicated. However, the inputs suggested against requiring a previous trial of anticholinergics or apomorphine preparations for reimbursement of foslevodopa-foscarbidopa. The clinician group inputs agreed with the clinical expert that treatment response would be assessed based on

off time, presence of disabling dyskinesia, and quality of life, and added that an association with easing of burden on partners or caregivers may be considered. The clinician group inputs agreed that discontinuation could be considered in patients with intolerable AEs (e.g., skin reactions or hallucinations) and patients who are unable to use the pump properly due to cognitive decline related to disease progression or who lack caregiver support. The clinician group inputs agreed with the clinical experts that movement disorder neurologists, general neurologists, and geriatricians with experience in the treatment of PD would be comfortable and qualified to prescribe and maintain treatment with foslevodopa-foscarbidopa.

Drug Program Input

Input was obtained from the drug programs that participate in the CADTH Reimbursement Review process. The clinical experts consulted by CADTH provided advice on the potential implementation issues raised by the drug programs.

Table 2: Responses to Questions From the Drug Programs

Implementation issues	Response
Relevant comparators	
There are 2 clinical studies: **M15-736** • Phase III, randomized, double-blind, double-dummy, active-controlled, parallel-group multicentre study • Comparator is carbidopa-levodopa IR tabs **M15-741** • Phase III, open-label, single-arm, multicentre study • No comparator 1. Should LCIG (Duodopa) have been used as a comparator in the clinical studies? 2. Should DBS have been used as a comparator in the clinical studies?	CDEC agreed with the clinical experts that LCIG and DBS are relevant comparators for foslevodopa-foscarbidopa because all 3 treatments would generally be considered options for those who do not have satisfactory control of PD motor symptoms despite optimized treatment with other oral PD medications. The clinical expert had no major concern with the lack of direct comparison of foslevodopa-foscarbidopa with these treatments. It was the clinical expert's opinion that the M15-736 trial of foslevodopa-foscarbidopa had a similar study design as a pivotal trial of LCIG (i.e., double-dummy, active-controlled design, with optimized oral therapy as the comparator) and could similarly provide evidence for the efficacy of foslevodopa-foscarbidopa.
1. If the patient is a candidate for DBS and the procedure is available, should the patient receive DBS rather than foslevodopa-foscarbidopa or LCIG (i.e., the efficacy and safety of DBS is probably superior to drug therapy in most patients)? 2. If the patient does not respond to or loses response to DBS, would they be an appropriate candidate for foslevodopa-foscarbidopa? 3. Is it reasonable to use foslevodopa-foscarbidopa in a patient who needs to wait a significant time period (e.g., > 1 year) to receive DBS? 4. If the patient does not respond to, loses response to, or is intolerant of LCIG, would they be an appropriate candidate for foslevodopa-foscarbidopa? 5. Is there still a role for LCIG if foslevodopa-foscarbidopa is available? If so, in which patients?	1. The clinical expert noted that the comparative efficacy for DBS vs. LCIG has not been well established; however, the clinical expert's opinion was that these treatments are expected to have similar efficacy for treating motor symptoms. • In the clinical expert's opinion, efficacy should not be the only clinical factor that guides treatment choice; patient preference and health system factors must also be taken into consideration. 2. CDEC agreed with the clinical expert that patients who do not respond to or lose response to DBS could be candidates for foslevodopa-foscarbidopa. 3. The clinical expert noted that for patients who have a long wait time for DBS surgical consult, treatment with foslevodopa-foscarbidopa could provide benefits with symptoms and quality of life and be initiated within weeks or months. 4. CDEC agreed with the clinical expert that foslevodopa--

Implementation issues	Response
	foscarbidopa could be considered in patients who respond to LCIG treatment but develop tube complications or a new medical issue that renders LCIG treatment no longer appropriate. 5. CDEC agreed with the clinical expert that although most patients would likely prefer the simplicity of SC infusion of foslevodopa-foscarbidopa over the PEG-J tube insertion required for LCIG, some patients with poor tolerability to foslevodopa-foscarbidopa may consider LCIG as an alternative option.
Considerations for initiation of therapy	
The inclusion criteria of M15-736 are the following: • ≥ 30 years of age • diagnosis of levodopa-responsive idiopathic PD that is inadequately controlled by current therapy • taking ≥ 400 mg/day levodopa equivalents • must have motor fluctuations (on/off) • average ≥ 2.5 hours per day off for 3 consecutive days before enrolment • ≥ 2 hours per day off for 3 consecutive days before randomization • MMSE score ≥ 24 • able to demonstrate correct understanding and use of the delivery system (patient or caregiver). Should any of these inclusion criteria in M15-736 be used as reimbursement criteria?	The clinical expert noted that the following criteria would be reasonable for the reimbursement of foslevodopa-foscarbidopa: • ≥ 18 years of age • diagnosis of levodopa-responsive idiopathic PD that is inadequately controlled by current therapy • must have motor fluctuations (on/off) • average ≥ 2.5 hours per day of off time (with ≥ 2 hours each day) despite best medical therapy as determined by the treating neurologist • able to demonstrate correct understanding and use of the delivery system (patient or caregiver). According to the clinical expert, there could be rare scenarios in which the onset of PD occurred before the age of 30 years. Further, 400 mg/day of levodopa equivalents is generally considered a low dose, and most patients who pursue advanced PD therapies have higher daily dose requirements due to severity of disease. Patients with cognitive impairment should not be excluded from treatment because cognitive impairment is not a medical contraindication to foslevodopa-foscarbidopa, although it may not be clinically appropriate to pursue advanced therapy in general in patients with severe cognitive impairment or dementia because of a likelihood of pulling out the connecting tube or wire due to confusion. CDEC agreed that the criteria noted by the clinical expert are reasonable and noted that they are in line with the reimbursement criteria for LCIG for most public drug plans at the time of the review.
The public drug plans who reimburse LCIG have roughly the same initiation criteria, which are as follows: 1. The patient has not been able to achieve satisfactory control of severe, debilitating motor fluctuations and hyperkinesia or dyskinesia despite optimized treatment with available combinations of PD treatments, including maximally tolerated doses of levodopa in combination with carbidopa, a COMT inhibitor, a dopamine agonist, a MAO-B inhibitor, and amantadine, if not contraindicated. 2. The patient experiences severe disability associated	CDEC agreed with the clinical expert that the initiation criteria for LCIG stated (except for number 4) would be applicable to foslevodopa-foscarbidopa. CDEC noted that it would also be reasonable to require the patient or caregiver to demonstrate correct understanding and use of the delivery system for reimbursement of foslevodopa-foscarbidopa treatment.

Implementation issues	Response
with at least 25% of the waking day in the off state and/or ongoing, bothersome levodopa-induced dyskinesias despite having tried frequent dosing of levodopa (at least 5 doses per day) 3. The patient has received an adequate trial of maximally tolerated doses of levodopa, with demonstrated clinical response. 4. The benefits of using LCIG treatment outweigh the risks associated with the insertion and long-term use of the PEG-J tube required for administration AND the patient does not have severe psychosis or dementia. Are these initiation criteria (with the exception of number 4) for LCIG still clinically appropriate and could they be used for foslevodopa-foscarbidopa?	
Considerations for continuation or renewal of therapy	
The public drug plans who reimburse LCIG have roughly the same renewal criteria, which are as follows: • The patient continues to benefit from the treatment, including significant reduction in the time spent in the off state and/or in ongoing, bothersome levodopa-induced dyskinesias, along with an improvement in the severity of the disability in the off state. • The duration of approval is 1 year. Are these renewal criteria for LCIG still clinically appropriate for use with foslevodopa-foscarbidopa? If so, could they be used for foslevodopa-foscarbidopa?	CDEC agreed with the clinical expert that the renewal criteria for LCIG would be applicable to foslevodopa-foscarbidopa.
Considerations for discontinuation of therapy	
Some public drug plans who reimburse LCIG have the following discontinuation criterion: • It is expected that physicians will continue to monitor their patients and discontinue LCIG if the patient is no longer benefiting from treatment, as described for renewal criteria, or if LCIG is no longer appropriate. Is this discontinuation criterion for LCIG still clinically appropriate for use with foslevodopa-foscarbidopa? If so, could it be used for foslevodopa-foscarbidopa?	CDEC agreed with the clinical experts that the discontinuation criterion for LCIG would be applicable to foslevodopa-foscarbidopa.
Considerations for prescribing of therapy	
Most public drug plans who reimburse LCIG restrict prescribing to movement disorder specialists. Should foslevodopa-foscarbidopa reimbursement be restricted to prescribers specialized in movement disorders?	The clinical expert noted that restricting prescribing of foslevodopa-foscarbidopa to prescribers specialized in movement disorders would be appropriate in most cases. However, in rural or remote areas, neurologists who are sufficiently experienced, qualified, and trained to administer and monitor foslevodopa-foscarbidopa treatment might not be available. As such, specifying a movement disorder specialist in the prescribing condition would create a barrier to accessing the treatment for those patients. The clinical expert preferred to leave the prescribing condition broad by allowing prescribing by

Implementation issues	Response
	neurologists who have experience in the treatment of patients with PD to prescribe foslevodopa-foscarbidopa. CDEC has recommended the prescribing criteria in Table 1.
Care provision issues	
Foslevodopa-foscarbidopa needs to be drawn from a vial using a syringe and then loaded into an AbbVie trademarked pump (Vyafuser) to be continuously infused into the subcutaneous tissue 24 hours a day. Do you have experience with the administration of this drug? Are patients with PD able to manage this?	The clinical expert did not foresee the infusion system to be a major barrier to receiving treatment. Based on the clinical expert's experience with LCIG, there is generally adequate training involved, and movement disorder specialists are attuned to the need for patients and caregivers to be able to operate the device. Additional support could also be provided to patients or families who could not manage the infusion device reliably. The clinical expert expected the administration of foslevodopa-foscarbidopa to be less of an issue compared with LCIG, for which setting up, cleaning, flushing, and turning on the pump and PEG-J tubing could be difficult when patients are in the off state and have poor motor symptoms.
The longest study was M15-741 at 52 weeks. Are there side effects with long-term continuous subcutaneous infusion of foslevodopa-foscarbidopa that should be monitored?	The clinical expert noted that there is some interest in whether there could be concerns related to deficiencies in B vitamins with foslevodopa-foscarbidopa (as are monitored for patients on LCIG), although clinicians have had challenges with obtaining approval for ordering some of these laboratory tests.

CDEC = CADTH Canadian Drug Expert Committee; COMT = catechol-O-methyl transferase; DBS = deep brain stimulation; IR = immediate release; LCIG = levodopa-carbidopa intestinal gel; MAO-B = monoamine oxidase B; MMSE = Mini-Mental State Exam; PD = Parkinson disease; PEG-J = percutaneous endoscopic gastrostomy-jejunostomy.

Clinical Evidence

Pivotal Studies and RCT Evidence

Description of Studies

The sponsor submitted 1 pivotal phase III, double-blind, double-dummy RCT (M15-736, N = 141), which assessed whether individualized foslevodopa-foscarbidopa continuous subcutaneous infusion increased change from baseline in average daily normalized on time without troublesome dyskinesia compared to oral LD-CD immediate release tablet therapy after 12 weeks in patients with PD with motor fluctuations inadequately controlled by oral therapy. Patients with prior DBS or LCIG treatment were excluded, and eligibility for DBS was not a consideration for enrolment. Study-defined key secondary end points included change from baseline in average daily normalized off time, Movement Disorder Society-Unified Parkinson's Disease Rating Scale (MDS-UPDRS) part II score, and presence of morning akinesia. Secondary end points included on time without dyskinesia and other measures of symptoms and health-related quality of life (HRQoL) (PD Questionnaire-39 items [PDQ-39], EQ-5D-5L, median and interquartile range of bradykinesia and dyskinesia scores assessed by the Parkinson KinetiGraph/Personal KinetiGraph [PKG] device, and Parkinson's Disease Sleep Scale-2 [PDSS-2]).

At baseline, patients had a mean age of 66.4 years (standard deviation [SD] = 9.5 years), and the majority of patients were male and white. Mean time since diagnosis of PD was 8.6 years (SD = 4.9 years). Mean off

time and on without troublesome dyskinesia time per day was 6.13 hours (SD = 2.097 hours) and 9.34 hours (SD = 2.514 hours), respectively.

Efficacy Results

On Time Without Troublesome Dyskinesia

The least-square (LS) mean difference between the foslevodopa-foscarbidopa arm and the oral LD-CD arm with respect to change from baseline to week 12 in average daily normalized on time without troublesome dyskinesia (primary end point) was 1.75 hours (95% CI, 0.46 to 3.05 hours; P = 0.0083) in favour of foslevodopa-foscarbidopa. Results of the sensitivity analyses assessing the impact of attrition and results of subgroup analyses of interest (age, duration of PD diagnosis, and levodopa dose intensity) were consistent with the primary analysis.

Off Time

The LS mean difference between the foslevodopa-foscarbidopa arm and the oral LD-CD arm with respect to change from baseline to week 12 in average daily normalized off time (study-defined key secondary end point) was −1.79 hours (95% CI, −3.03 to −0.54 hours, P = 0.0054) in favour of foslevodopa-foscarbidopa. Results of the sensitivity analyses assessing the impact of attrition and subgroup analyses of interest were consistent with the primary analysis.

PD Questionnaire-39 Items (PD-Specific HRQoL Instrument)

The LS mean difference between the foslevodopa-foscarbidopa arm and the oral LD-CD arm with respect to change from baseline to week 12 in the PDQ-39 summary index (secondary end point) was −4.10 (95% CI, −8.14 to −0.05). The results for this outcome are at increased risk of type I error (false-positive results) because they were tested after failure of the statistical hierarchy.

Movement Disorder Society-Unified Parkinson's Disease Rating Scale Part II Score (Motor Experiences of Daily Living)

The LS mean difference between the foslevodopa-foscarbidopa arm and the oral LD-CD arm with respect to change from baseline to week 12 in MDS-UPDRS Part II score (study-defined key secondary outcome) was −1.58 (95% CI, −3.65 to 0.48; P = 0.13).

Parkinson's Disease Sleep Scale-2

The LS mean difference between the foslevodopa-foscarbidopa arm and the oral LD-CD arm in change from baseline to week 12 in PDSS-2 total score (secondary end point) was −5.40 (95% CI, −8.03 to −2.78). The results for this outcome are at increased risk of type I error (false-positive results) because they were tested after failure of the statistical hierarchy.

Adverse Events

Treatment-emergent adverse events (TEAEs) were reported in 85.1% of patients in the foslevodopa-foscarbidopa arm, and 62.7% of patients in the oral LD-CD arm. The most common TEAEs in the foslevodopa-foscarbidopa arm (at least 10%) were infusion site erythema, pain, cellulitis and edema, as well as dyskinesia, all of which were more commonly reported than in the oral LD-CD arm (infusion site

erythema and pain: 1.5% each). The frequency of falls was lower in the foslevodopa-foscarbidopa arm (8.1%) compared with the oral LD-CD arm (17.9%).

Serious Adverse Events

Serious TEAEs were reported in 6 (8.1%) patients in the foslevodopa-foscarbidopa arm and 4 (6.0%) patients in the oral LD-CD arm.

Withdrawals Due to Adverse Events

Treatment discontinuation due to a TEAE was reported in 21.6% of patients in the foslevodopa-foscarbidopa arm and 1.5% of patients in the oral LD-CD arm. The most common TEAEs leading to treatment discontinuation in the foslevodopa-foscarbidopa arm were infusion site cellulitis (5.4%), infusion site pain (4.1%), and infusion site bruising, hemorrhage, and edema (2.7% each).

Mortality

No deaths were reported in the foslevodopa-foscarbidopa arm, and 1 (1.5%) death was reported in the oral LD-CD arm.

Notable Harms

The frequency of infusion site reactions and infusion site infections were notably higher in the foslevodopa-foscarbidopa arm compared with the oral LD-CD arm (infusion site reactions: 62.2% versus 7.5%; infusion site infections: 28.4% versus 3.0%).

The frequency of hallucination or psychosis was notably higher in the foslevodopa-foscarbidopa arm (14.9%) compared with the oral LD-CD arm (3.0%). Impulsive-control disorder or impulsive behaviour were not reported in either treatment arm. There was no notable between-arm difference in the mean change from baseline in score for each impulse control disorder and related behaviour parameters of the Questionnaire for Impulsive-Compulsive Disorders in Parkinson Disease Rating Scale (QUIP-RS) across almost all time points. Based on the Columbia-Suicide Severity Rating Scale (C-SSRS) assessment, 5 (6.8%) patients in the foslevodopa-foscarbidopa arm and 2 (3.0%) patients in the oral LD-CD arm had suicidal behaviours or ideations. Depression was reported in zero patients in the foslevodopa-foscarbidopa arm, and 2 (3.0%) patients in the oral LD-CD arm.

Dizziness was reported in 3 patients in either treatment arm. Orthostatic hypotension by preferred term was reported in 1 (1.4%) patient in the foslevodopa-foscarbidopa arm and 2 (3.0%) patients in the oral LD-CD arm. Somnolence was reported in 1 (1.4%) patient in both treatment arms.

Critical Appraisal

Results of an end-of-study survey aiming to assess the extent of unblinding suggested that the majority of patients were able to infer treatment assignment given the differences in treatment response. There is a risk of reporting bias from patients for patient-reported outcomes that is potentially in favour of foslevodopa-foscarbidopa due to the subjective nature of these outcomes. However, the extent of bias is unclear. Further, although a hierarchical testing procedure was in place to account for multiplicity, no definitive conclusion can be drawn with respect to end points other than the primary end point, and study-defined key secondary end

points of off time, as well as MDS-UPDRS part II score, due to a failure of statistical comparison in a prior end point in the testing hierarchy (i.e., MDS-UPDRS part II score). No conclusion can be drawn on the prespecified subgroup analyses due to the lack of sample size consideration and control for multiplicity. As well, there was a risk of attrition bias in favour of foslevodopa-foscarbidopa due to higher attrition in the foslevodopa-foscarbidopa arm compared with the oral LD-CD arm; however, sensitivity analyses of the primary end point and the key secondary end point of off time, which assessed the impact of missing data, showed results consistent with the primary analysis, increasing certainty of the findings.

Patients with cognitive impairment and prior DBS or LCIG treatment were excluded from the study, which represents a gap in evidence; nonetheless, the clinical expert consulted by CADTH did not expect the exclusion of these patients to significantly impact the generalizability of the study population. With respect to outcomes, the clinical expert noted that the PD diary, MDS-UPDRS, and PDQ-39 are clinically relevant instruments used in clinical practice, whereas the relevance of bradykinesia and dyskinesia scores, EQ-5D-5L score, and PDSS-2 score are limited. Improved cognition was an unmet treatment need according to patients, and reduced caregiver burden is a treatment goal in advanced PD. No conclusion about these outcomes can be drawn from the study because the former outcome was not assessed as a stand-alone end point (although captured as 1 of the items in MDS-UPDRS scale) and the latter outcome was not measured. The clinical expert noted that the duration of follow-up (12 weeks) was adequate for efficacy assessment, although longer follow-up is required to gain certainty on the maintenance of benefit and safety profile.

Long-Term Extension Studies

The M20-098 trial is an ongoing long-term, open-label extension study of the pivotal RCT previously described (M15-736) in which patients received individualized foslevodopa-foscarbidopa continuous subcutaneous infusion 24 hours per day for up to 96 weeks. At the time of the submission, no patients had completed the trial, and data were available from fewer than 5 patients from week 24 and beyond for outcomes of interest. Therefore, the data from M20-098 were too immature to draw conclusions from.

Indirect Comparisons

Description of Indirect Comparisons

The sponsor's submission included 1 sponsor-conducted indirect treatment comparison, which indirectly compared foslevodopa-foscarbidopa with LCIG and best medical therapy (oral therapy) with respect to change from baseline in mean off time, on time without troublesome dyskinesia, and PDSS-2 total score at week 12 in patients with advanced PD via a Bayesian NMA.

Efficacy Results

In the Bayesian fixed-effect NMA, which was based on a total of 4 trials, foslevodopa-foscarbidopa, compared with best medical therapy (oral therapy), was associated with improved mean change from baseline at week 12 in average on time without troublesome dyskinesia (mean difference, [redacted]) hours, off time (mean difference, [redacted]) hours, and PDSS-2 total score (mean difference, [redacted]). Compared with LCIG, foslevodopa-foscarbidopa was associated with an improvement with change from baseline at week 12 in PDSS-2 total score (LCIG versus foslevodopa-

foscarbidopa: mean difference, [redacted]) and no difference in on time without troublesome dyskinesia (mean difference, [redacted]) hours and off time (mean difference, [redacted]) hours.

Critical Appraisal

The validity of the results of the NMA could not be determined because the key assumptions of the analysis, homogeneity, and consistency could not be determined based on insufficient reporting of study characteristics and a sparse linear network without a closed loop. Based on the available information, there was evidence of heterogeneity between the included studies based on study designs (i.e., blinding, dosing protocol for oral therapies, duration of follow-up), patient populations (i.e., presence of concurrent cognitive impairment and dyskinesia), and patient baseline characteristics (i.e., duration of PD diagnosis, off time) that were unaccounted for. These limitations result in uncertainty in the relative treatment effect estimates between foslevodopa-foscarbidopa versus best medical therapy (oral therapy) and LCIG.

Studies Addressing Gaps in the Pivotal and RCT Evidence

M15-741 Trial

One supportive phase III, open-label, single-arm trial (M15-741; N = 244) that aimed to evaluate the safety and tolerability of foslevodopa-foscarbidopa in patients with advanced PD for 52 weeks, was included in the sponsor's submission. Safety and efficacy were assessed as primary and secondary end points, respectively, most of which were consistent with the end points in the M15-736 trial. Baseline patient characteristics were similar to the M15-736 trial, although mean time since PD diagnosis (mean = 12.3 years; SD = 5.3 years) was longer in the M15-741 trial and more patients were at advanced stages of PD (based on the Hoehn and Yahr scale) and received, on average, more medications from different PD drug classes. These suggest that the patient population in the M15-741 trial had more advanced disease than the patient population included in the M15-736 trial.

Efficacy Results

All efficacy results were not adjusted for multiplicity. Foslevodopa-foscarbidopa was associated with a statistically significant improvement from baseline in average daily normalized on time without troublesome dyskinesia ([redacted]), off time ([redacted]), on time without dyskinesia ([redacted]), PDQ-39 ([redacted]), MDS-UPDRS part II score ([redacted]) and IV score ([redacted]), PDSS-2 total score ([redacted]), and EQ-5D-5L summary index ([redacted]) at 52 weeks. Results did not suggest a difference in change from baseline in MDS-UPDRS part I and III scores, as well the medians and interquartile ranges of bradykinesia scores and dyskinesia scores at week 52 with foslevodopa-foscarbidopa treatment.

Harms Results

TEAEs were reported in [redacted]. The safety profile of foslevodopa-foscarbidopa in this trial was generally consistent with the M15-736 trial, with no new safety signal.

Critical Appraisal

The open-label study design could introduce reporting bias, potentially leading to inflated benefits of foslevodopa-foscarbidopa on patient-reported outcomes and less favourable harms results given the more subjective nature of these outcomes. The noncomparative design means that known and unknown confounding factors were not accounted for and no statistical adjustments were made in the analyses, making it impossible to be certain that the observed treatment benefits could be attributed to foslevodopa-foscarbidopa alone [redacted]. As a result, attrition bias may explain the observed efficacy results because patients who remained in the study were more likely to be those who experienced benefits and were able to tolerate the treatment better.

The inclusion and exclusion criteria generally align with the selection criteria for candidates for advanced therapies used in clinical practice. Although patients included in this trial appeared to have more advanced PD than those in the pivotal M15-736 trial, the clinical expert noted that the patient population would fit within the spectrum of patients with advanced PD in Canada. [redacted]. This could potentially affect the generalizability of the results because patients who remained in the trial tended to be those who tolerated AEs associated with foslevodopa-foscarbidopa better. The difference in infusion systems used in the trial versus stated in the product monograph could introduce some uncertainty due to potential differences in treatment interruptions, adherence, and safety.

M15-737 Trial

Early results from the ongoing single-arm, long-term, open-label extension M15-737 trial were submitted by the sponsor and are summarized in this report. Patients who completed the M15-741 trial could enrol in the M15-737 trial. The objective of the M15-737 trial is to assess the longer-term safety and tolerability of foslevodopa-foscarbidopa delivered by continuous subcutaneous infusion for 24 hours per day for up to an additional 96 weeks after the 52-week M15-741 trial. The primary outcomes are AEs and safety measures. Efficacy outcomes are also being collected as secondary end points. At the time of this submission, data were limited after 48 weeks, and no patients had yet completed the study.

Efficacy Results

[redacted]

Harms Results

[redacted]

Critical Appraisal

The open-label study design could introduce reporting bias, potentially leading to inflated benefits of foslevodopa-foscarbidopa on patient-reported outcomes and less favourable harms results given the

more subjective nature of these outcomes. The noncomparative design means that known and unknown confounding factors were not accounted for, and no statistical adjustments were made in the analyses, making it impossible to be certain that the observed treatment benefits could be attributed to foslevodopa-foscarbidopa alone. Because patients could only enrol after completion of the parent study, there is a greater likelihood of selection bias given that patients who better tolerated the treatment or perceived the treatment to be benefiting them were more likely to enrol. Finally, the trial is ongoing, and data are limited after week 48. At the available time points, sample sizes are small. No definitive conclusions could be drawn from the results of this study.

Economic Evidence

Table 3: Cost and Cost-Effectiveness

Component	Description
Type of economic evaluation	Cost-minimization analysis
Target population	Adult patients with PD whose symptoms are not adequately controlled on optimized oral therapies (advanced PD) and who are not candidates for DBS
Treatment	Foslevodopa-foscarbidopa with adjunctive therapy
Dosing regimen	1 vial per day, for a total of 365.25 administrations per year
Submitted price	Foslevodopa-foscarbidopa, 2,400 mg foslevodopa and 120 mg foscarbidopa, solution for SC infusion: $169.81 per single-use vial
Treatment cost	$62,023 annually
Comparator	LCIG with adjunctive therapy
Perspective	Canadian publicly funded health care payer
Time horizon	Lifetime (20 years)
Key data source	A sponsor-commissioned indirect treatment comparison using Bayesian network meta-analysis was conducted to compare the relative clinical efficacy between foslevodopa-foscarbidopa and LCIG
Costs considered	Drug acquisition costs, administration costs, and surgical costs
Key limitations	• The sponsor's reimbursement request to exclude patients who are candidates for DBS was noted as a limitation by the clinician expert consulted for this review because foslevodopa-foscarbidopa may be used in patients who are candidates for DBS. The clinical effectiveness and cost-effectiveness of foslevodopa-foscarbidopa relative to DBS are unknown. • Feedback from the clinical expert noted that, although some patients with advanced PD may receive advanced therapies such as DBS or LCIG, most patients would remain on oral therapy despite inadequate control of motor symptoms. Therefore, exclusion of oral levodopa-carbidopa as a relevant comparator was not appropriate. • The comparative clinical effectiveness of foslevodopa-foscarbidopa to LCIG is uncertain because of the limitations in the sponsor-submitted network meta-analysis. Limitations included a sparse network, the absence of closed loop which rendered a consistency assessment infeasible, and unaccounted heterogeneity in study designs, patient populations, and baseline characteristics. • Administration costs in the sponsor's cost-minimization analysis included only titration and monitoring

Component	Description
	costs associated with both foslevodopa-foscarbidopa and LCIG. Clinical expert feedback obtained by CADTH noted that several other administration costs were missing from the sponsor's submission. This included gastroenterology consults, an ambulatory care visit for a gastroscopy procedure, and personnel costs. Furthermore, included surgery costs were inaccurately calculated or inflated in the sponsor's base case.
CADTH reanalysis results	• CADTH corrected the sponsor's base case by updating the surgical costs associated with LCIG administration. In this reanalysis, foslevodopa-foscarbidopa was associated with cost-savings of $2,453.03 in year 1 and remained cost neutral for the rest of the 20-year time horizon (i.e., no cost difference). • Because the drug acquisition costs for foslevodopa-foscarbidopa are the same as LCIG, a price reduction was not completed. The analysis was conducted based on the public list price of LCIG because the confidentially negotiated price of LCIG is unknown.

DBS = deep brain stimulation; LCIG = levodopa-carbidopa intestinal gel; PD = Parkinson disease.

Budget Impact

CADTH identified the following key limitations from the sponsor's analysis: exclusion of DBS as a relevant comparator in the budget impact analysis and the sponsor underestimated the market uptake of foslevodopa-foscarbidopa. CADTH did not conduct a base-case analysis because the sponsor's submission provided adequate presentation of the budget impact for foslevodopa-foscarbidopa. CADTH presented a series of scenario analyses to test the impact of alternative assumptions on the estimated budget impact and provided corrections to the existing sponsor-submitted scenario analysis. The sponsor's base case suggested the reimbursement of foslevodopa-foscarbidopa is associated with a 3-year budgetary impact of $0. When considering surgical costs, the 3-year budgetary impact resulted in cost-savings of $296,539. Because the explored analyses all assumed that the reimbursement of foslevodopa-foscarbidopa would only displace LCIG, the budget impact of foslevodopa-foscarbidopa taking market share from non-LCIG therapies is unknown.

CDEC Information

Members of the Committee

Dr. James Silvius (Chair), Dr. Sally Bean, Mr. Dan Dunsky, Dr. Alun Edwards, Mr. Bob Gagne, Dr. Ran Goldman, Dr. Allan Grill, Mr. Morris Joseph, Dr. Christine Leong, Dr. Kerry Mansell, Dr. Alicia McCallum, Dr. Srinivas Murthy, Ms. Heather Neville, Dr. Danyaal Raza, Dr. Emily Reynen, and Dr. Peter Zed.

Meeting date: April 26, 2023

Regrets: One expert committee member did not attend.

Conflicts of interest: None