

Decision Aid Tool

Whether or not to take levodopa-carbidopa intestinal gel (LCIG) to control the symptoms of Parkinson's disease (PD)



This document is intended for:

- persons with Parkinson's disease (PD) whose motor symptoms are poorly controlled with oral medication and in whom treatment with levodopa/carbidopa intestinal gel (LCIG) may be indicated;
- close relatives of these persons, if applicable.



This document is meant to:

- inform the persons affected about this treatment option;
- prepare them to discuss these with health professionals;
- help them choose what appears to them to be the best option.

We recommend that:

- the decision takes into consideration the person's values and priorities;
- the decision is shared between the health professional, person affected and caregiver.

WHAT ARE MY CHOICES?

<p>TO TAKE levodopa/carbidopa intestinal gel (LCIG)</p>	
<p>NOT TO TAKE levodopa/carbidopa intestinal gel (LCIG)</p> <p>Discuss other possible treatments with the neurologist (continue oral medication, take additional medication as needed or consider other advanced treatment such as deep brain stimulation)</p>	

PRACTICAL ASPECTS OF LCIG TREATMENT

Pre-treatment evaluations

Treatment with LCIG is considered when the neurologist judges that the oral treatments attempted to date are no longer able to control motor fluctuations satisfactorily. Before beginning treatment, it is important to ensure that there are no contraindications. Additional tests may be requested as well as a meeting with a gastroenterologist.

Mode of administration

LCIG is administered with a portable pump connected to a tube installed through the abdominal wall into the small intestine (gastrojejunal tube). As the drug is administered continuously and directly into the intestine, this enables more regular absorption and more stable concentrations of the drug in the blood and brain.

The pump ensures continuous administration of a programmed dose of the drug over a period of approximately 16 hours a day. In cases where symptoms are poorly controlled overnight, however, some people may benefit from a treatment of up to 24 hours. LCIG generally replaces the need for several oral anti-Parkinson's drugs.

Start of treatment

All instructions regarding the use of the medication and the pump are given before and during the initiation of treatment. Related documents are provided as a reference. It is recommended to consult them.

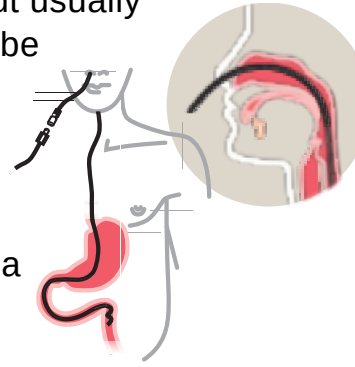
Treatment is personalized after discussion with the neurologist. The initial doses to be administered are calculated based on oral doses of levodopa/carbidopa taken daily: **morning dose***, **continuous maintenance dose***, and **extra dose (or bolus*)**. All instructions regarding the use of the pump are given before and during the start of treatment. Related documents are provided as a reference.

Treatment may be started:

- in one or two stages;
- in an external clinic or during a short hospital stay;
- the same day as the nasojejunal tube or gastrojejunal tube is installed, or in the following days.

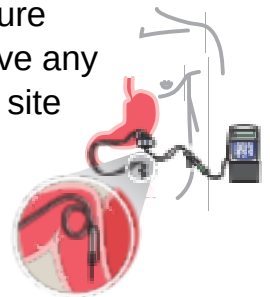
* See the glossary on p. 9

1) A trial period for the drug may be suggested. This period can vary but usually does not exceed four weeks. The drug is administered via a soft nasal tube that descends into the small intestine. This tube is installed by a **gastroenterologist*** in an **endoscopy*** suite. A **mild sedative*** is administered to help the patient better tolerate the procedure. This trial period makes it possible to see the effects of the drug on motor and non motor symptoms before installing the gastrojejunal tube. It also provides a period of adaptation to the new mode of administering the drug.



If, after the trial period, the person does not wish to continue with the treatment, he or she can decide not to move to the second stage. The nasojejunal tube is simply removed by a health professional, and the previous oral treatments are resumed.

2) The gastrojejunal tube can also be installed directly, thereby omitting the trial period with the nasojejunal tube. The procedure is usually performed by a **gastroenterologist*** in an **endoscopy*** suite. A **mild sedative*** is administered before the procedure to prevent infection. An analgesic may be prescribed for several days to relieve any pain that may result from the procedure. A bandage is placed at the insertion site of the tube.



The tube is not permanent. It may be removed or replaced as needed by a physician. If handled properly, the tube may remain in place for five years. A change may be requested for preventative reasons. Currently, there is no consensus on the frequency at which the tube should be changed.

Dosage adjustment

Follow-ups are done in clinic, then eventually remotely, to adjust the dose of the drug until optimal control of symptoms is achieved. The person can also self-administer an additional dose (called a bolus) in the event of **OFF*** time or temporarily stop the pump in the event of **dyskinesia***. In addition to the neurologist and specialized nursing staff that provide close follow-up, a member of the assistance program sponsored by the manufacturer is available to answer questions.

Levodopa/carbidopa intestinal gel (LCIG)

The drug is contained in a plastic cassette away from light and must be kept cool at between 2°C and 8°C. Since several cassettes are delivered at one time, a second refrigerator is sometimes useful to store them. The treatment was approved by Sweden in 2004 and was made available in Canada in 2013.

Daily routine

Here is an overview of the daily routine of a person treated with LCIG:

* See the glossary on p. 9

Upon awakening:

- A new medication cassette is attached to the pump and then the cassette tube is connected to the gastro-jejunal tube.
- A pre-programmed morning dose is administered by pressing a button on the pump. The pump then automatically switches to continuous medication delivery.

During the day:

- As soon as the effects of the medication are felt (in about 15-20 minutes), the person can carry out daily activities, hobbies and sports. Different methods of carrying the pump can be used (jacket, waist belt, shoulder bag etc.).
- The pump can be temporarily disconnected while showering, bathing or swimming.
- A visual inspection and gentle cleaning is done around the catheter insertion point to ensure the skin's integrity. This can be done as part of the daily bathing routine.

At bedtime:

- The pump is switched to off mode and disconnected from the gastro-jejunal tube.
- The probe is flushed with tap water using a syringe with an adapter to ensure permeability.

Cost

The daily cost of LCIG treatment is approximately CAN\$166.00. However, private or public insurance plans cover most of the cost. If you have private insurance, the amount to be paid depends on your plan. In the case of public plans, drug coverage varies between provinces and territories.

To ensure maximum coverage, the support program sponsored by the manufacturer offers each LCIG user help with the drug reimbursement process (which can be complex).

LEVELS OF SCIENTIFIC EVIDENCE

Information about the advantages and disadvantages of LCIG, along with patients' experience with the product, are accompanied by a pyramid symbolizing the level of scientific evidence. These levels of evidence refer to the ways studies have been conducted with research participants. They are graduated based on the scientific value of the conclusions. The higher the level of evidence is, the less likely new research will change the conclusions. In this document, the levels of evidence are identified, as follows:



High



Moderate



Low



Absence of data

* See the glossary on p. 9

EFFECTS OF LCIG ON PERSONS WITH PARKINSON'S DISEASE

ADVANTAGES OF THE TREATMENT



↓ Motor symptoms

After starting LCIG:

- **"OFF"** times decrease by an average of 4 hours per day
- **"ON"** times without **dyskinesia*** increase by an average of 4 hours per day
- Balance and gait are improved for up to 4 years

↓ Non-motor symptoms

People treated with LCIG can achieve significant improvement in the following areas:

- Mood
- Cognition/memory
- Sleep
- Urinary symptoms
- Gastrointestinal symptoms
- Impulsive behaviour

↑ Quality of life

Persons treated with LCIG can experience significant improvements in their quality of life for up to 3 years after starting treatment.

DISADVANTAGES OF THE TREATMENT



= Adverse events of the drug

- Since LCIG is levodopa-carbidopa (as in oral tablets), it may bring similar side effects such as:
 - Hallucinations, confusion,
 - Psychotic disorders,
 - Insomnia, falls
 - Dyskinesia, weight loss
 - Polyneuropathy
- However, people who use LCIG do not appear to have more or fewer side effects than those who receive the best oral treatment.

↑ Adverse events associated with the mode of administration

- Most persons using LCIG have **side effects*** related to its mode of administration. Most of them occur in the 2 to 4 weeks following the installation of the intestinal probe.
- The nature and intensity of these side effects are similar to those seen in people with gastrojejunal tubes for other reasons.
- The vast majority of side effects are minor, of mild to moderate intensity.

Side effects related to the installation of the probe

- The most frequent are :
 - Abdominal pain
 - Redness, oozing and infection
 - Excessive formation of **granulation tissue***

The more serious side effects* are :

- **Peritonitis***.
- Aspiration pneumonia
- Abdominal pain requiring hospitalization

Side effects related to the device

- The most common are:
 - Dislocation, displacement, occlusion or accidental removal of the tube;
 - Deterioration of the connectors

* See the glossary on p. 9



Autonomy in activities

As a result of the reduction in motor symptoms, people who use LCIG can have a significant improvement in their level of independence in everyday and leisure activities for up to 8 years after starting their treatment.

Replacement and removal of the tube

- One year after installation of their tube, 9 out of 100 persons had to have it replaced, and 37 had to have only the inner part replaced.
- One and a half years after installation of their tube, 4 out of 100 persons stopped LCIG treatment because of an adverse event related to the device.



ONE USER'S EXPERIENCE WITH LCIG



I'm lucky to have my wife. When I wake up in the morning, I'm too "OFF", so she helps me connect and start my pump. Once it's connected, I always feel "ON". I have more energy and motivation. I'm in a better mood because the product self administers at a regular and constant rate. I don't have to ask myself whether the next pill dose will be absorbed and work. When and what I eat doesn't worry me anymore. I can live a fairly normal life. I can even travel for several weeks since I can have my medication delivered. If I remove the pump, I can also go swimming.

Rewording of users' statements

The disadvantages are related to the pump itself. It is big and heavy. Carrying a 3 lb-load all day starts to pull on my neck or shoulder. And the equipment provided to carry the pump isn't very practical...I also need a second one in case the first one breaks. That's already happened. The batteries need to be changed every week and the tube needs to be flushed daily. It's also a problem getting dressed. I have trouble finding clothes that fit me, and it makes a lump under my coat. That's not very aesthetic. I also need to be careful when I go into the water. I have to be sure to remove the pump beforehand!

Rewording of users' statements

EFFECTS OF THE TREATMENT ON THE CAREGIVER

ADVANTAGES OF THE TREATMENT



Compared to the best oral treatments and other advanced treatments for PD, the caregiver of a person using LCIG:

- Feels that his or her quality of life is better.
- Tends to perceive a lesser workload.

DISADVANTAGES OF THE TREATMENT



The caregiver may need to alter his or her work or daily schedule to support the person using an advanced PD treatment, including LCIG.



CAREGIVER'S EXPERIENCE



My husband's disease is better controlled since he has been using LCIG. He is more mobile and independent. That gives me more time for myself. We've even started to do activities together again and to resume a more active social life. There are fewer side effects, such as dyskinesia, and when that does happen, we stop the pump for a few minutes, and it passes.

We don't have to constantly check our watch to make sure we don't forget a dose. And I'm not worried anymore when we leave the house. We're well supported logistically by our doctor and nurse. That helps reduce my stress. In hindsight, I feel there are more advantages than disadvantages for us with this treatment.

Rewording of users' statements

*When we started LCIG, I was worried. I realized that I would have to be there to help my wife manage the treatment because it's a little more complicated at first. The care that needed to be given every day, such as the **irrigation*** of the tube and the cleaning of the skin, stressed me out. I was afraid that the tube would tear off or that the pump would break. We had to try several ways of carrying the pump before finding the right one. We also had to adjust the doses more often.*

The other day, she went to the emergency department. The staff didn't know what to do with the pump. This treatment doesn't seem to be well known at the hospital. I had to explain it to them...

If I need to take a break outside the home, it's practically impossible. It takes someone who is trained and authorized to take care of the pump in my absence.

Rewording of users' statements

* See the glossary on p. 9

CHOOSING AN OPTION BASED ON YOUR PRIORITIES

CHECK OFF WHAT IS MOST IMPORTANT TO YOU AND YOUR CAREGIVER	OPTION TO CONSIDER
<input type="checkbox"/> I feel confident to try a new treatment to improve my motor symptoms even if the mode of administration is different.	Taking LCIG
<input type="checkbox"/> I don't want to try a treatment that requires a gastro-jejunal tube and daily care. This worries me too much.	Not taking LCIG
<input type="checkbox"/> I would like to improve my quality of life by not having to take medication at specific times, several times a day.	Taking LCIG
<input type="checkbox"/> I want to maintain my physical appearance and avoid having to wear a pump. I don't want it to show under my clothes and feel observed.	Not taking LCIG
<input type="checkbox"/> Other: _____	

In this exercise, the advantages and disadvantages of LCIG become priorities to consider. For example, avoiding a disadvantage could represent a priority for some people who would prefer not taking LCIG.

What option do you prefer? _____

ARE YOU COMFORTABLE WITH YOUR DECISION?

YES NO

S ure of myself	Do you feel SURE of the best choice for you?		
U nderstand information	Do you know the benefits and risks of each option?		
R isk-benefit ratio	Are you clear about which benefits and risks matter most to you?		
E ncouragement	Do you have enough support and advice to make a choice?		

SURE® test, O'Connor and Légaré, 2008

If you answered "NO" to one of the questions above, discuss this with your loved ones, neurologist or health professional specialized in the treatment of Parkinson's disease.

GLOSSARY – DEFINITIONS

Adverse event: Unwanted reaction caused by the administration of a health product (drug or treatment).

Continuous maintenance dose: Dose of levodopa/carbidopa gel administered (in mL/hour) when the pump is on.

Dyskinesia: Involuntary movements of one or several parts of the body generally caused by anti-Parkinson's medication.

Endoscopy: Visual examination conducted using an endoscope (tube fitted with a light) to make a diagnosis or perform a procedure or surgery. The upper gastrointestinal endoscopy makes it possible to examine the esophagus, stomach and a part of the small intestine.

Extra dose or bolus: Small dose administered as needed during the day (in mL).

Gastroenterologist: Physician specialized in diseases of the esophagus, stomach, intestines, liver, biliary tract and pancreas.

Granulation tissue: Bright red tissue, shiny and granular, that fills in and covers an open wound. When present in excessive amounts, it hinders healing.

Irrigation: Rinsing of the tube with water, using a syringe, to clean it and ensure its permeability.

Morning dose: Stronger dose administered in the morning when the pump is started up (in mL).

OFF: Period during which medication no longer controls motor and/or non-motor symptoms.

Peritonitis: Infection of the peritoneum, a fine membrane that covers the abdominal organs.

Sedation: Use of drugs to help a person relax or remain immobile during a test or treatment.

Serious adverse event: Reaction requiring hospitalization or extension of a hospital stay, which results in incapacitation or persistent or major disability, or is life-threatening or causes death.

DEVELOPMENT COMMITTEE

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Persons with Parkinson's disease, using or not using LCIG, caregivers and a nurse specialized in Parkinson's disease participated in developing this decision support tool.

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Distribution of the tool is permitted.
Any modification/adaptation must be approved by the authors.

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Kamel and Al-Hashel. (2020). *Brain and Behavior* ;10(9). Specifications: literature review, including 17 observational studies; Participants: 1,155; Treatment: LCIG; Follow-up: 2 to 48 months

Tsunemi *et al.* (2021). *Movement Disorders*. 36(8) : 1789-1771. Specifications : Systematic review including 56 studies : 1 systematic review, 1 randomized controlled study, 2 surveys and many observational studies. Participants : 6 709 ; Treatment : LCIG; Follow-up: 6 months to 10 years

Zhang *et al.* (2020). *Drug Design, Development and Therapy* ;14:845 854. Specifications: systemic review, including 3 randomized controlled studies and 2 randomized crossover studies; Participants: 198; Treatment: LCIG or oral drug; Follow-up: 7 to 54 weeks

Disadvantages of treatment for persons with Parkinson's disease

Antonini *et al.* (2021). *Advances in Therapy*, 38(6), 2854–2890. Specifications: Systematic review including 27 observational studies. Participants : 1 875; Treatment : LCIG; Follow-up: 1 year to 10 years

Zhang *et al.* (2020). *Drug Design, Development and Therapy*;14:845 854. Specifications: systematic review, including 3 randomized controlled studies and 2 randomized crossover studies; Participants: 198; Treatment: LCIG and/or oral drug; Follow-up: 7 to 54 weeks

Epstein *et al.* (2016). *Clinical and Translational Gastroenterology*;7(3):159. Specifications: systematic review, including 1 randomized controlled study and 3 observational studies; Participants: 395; Treatment: gastrojejunal tube for administration of LCIG or placebo; Follow-up: 12 months

Olanow *et al.* (2014). *The Lancet Neurology*;13(2):141-149. Specifications: randomized controlled study; Participants: 71; Treatment: LCIG or oral drug; Follow-up: 12 weeks

Experience of LCIG users and caregivers

The rewording of LCIG users' statements is based on the experience reported by users participating on the committee developing this tool and on the following work:

Canadian Agency for Drugs and Technologies in Health. (2018). Patient Input for Levodopa/Carbidopa (Duodopa); p. 26. Specifications: survey; Participants: 960 (persons with PD or caregivers); Treatment: LCIG.

Effects of treatment on caregivers

Tessitore *et al.* (2018). *Journal of Neurology*;265(5):1124-1137. Specifications: Cross-sectional observational study; Participants: 126 and their caregivers; Treatment: LCIG, oral treatment, continuous subcutaneous infusion of apomorphine or deep brain stimulation.

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