Package leaflet: Information for the user

Lecigon 20 mg/ml + 5 mg/ml + 20 mg/ml intestinal gel

levodopa/carbidopa monohydrate/entacapone

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

1. What Lecigon is and what it is used for
2. What you need to know before you use Lecigon
3. How to use Lecigon
4. Possible side effects
5. How to store Lecigon
6. Contents of the pack and other information

1. What Lecigon is and what it is used for

Lecigon is used for the treatment of Parkinson's disease. It is used in advanced cases when oral medicines (medicines taken by mouth) no longer produce sufficient effect.

Lecigon is a gel for continuous delivery that is supplied through a pump and tube directly into your small intestine. Lecigon contains three active substances:
- levodopa
- carbidopa (in the form of carbidopa monohydrate)
- entacapone

How Lecigon works
In a person with Parkinson's disease, the levels of dopamine in the brain are low. Levodopa is converted into dopamine in the brain, thereby relieving the symptoms of Parkinson's disease. Carbidopa and entacapone improve the effect that levodopa has on Parkinson's disease.

2. What you need to know before you use Lecigon

Do not use Lecigon if:
- You are allergic to levodopa, carbidopa, entacapone or any of the other ingredients in this medicine (listed in section 6).
- You have an eye problem called narrow-angle glaucoma (a type of glaucoma that is acute).
- You have severe heart failure.
- You have a severe irregular heartbeat (arrhythmia).
- You recently had a stroke.
- You have a serious liver disease.
- You are taking medicines for depression called selective MAO-A inhibitors (like moclobemide) and non-selective MAO inhibitors (like phenelzine). Treatment with these medicines must be discontinued at least two weeks before starting treatment with Lecigon. See also the section “Other medicines and Lecigon”.

- You have a tumour of the adrenal gland that causes overproduction of adrenaline and noradrenaline (pheochromocytoma).
- Your body produces too much cortisol (Cushing's syndrome).
- Your thyroid hormone levels are too high (hyperthyroidism).
- You have ever had neuroleptic malignant syndrome (a serious, rare reaction that can occur when being treated with or stopping use of certain medicines).
- You have ever had rhabdomyolysis (a severe, rare muscle condition that affects the kidneys), -
- You have ever had skin cancer, or you have any unusual moles or marks on your skin which have not been looked at by your doctor.

Warnings and precautions

Talk to your doctor **before using** Lecigon if you have or ever have had:

- a heart attack or any other cardiovascular disease, including angina and irregular heartbeat.
- asthma or any other lung problem.
- a kidney or liver disease.
- a hormone problem.
- a stomach ulcer.
- fits (convulsions).
- a serious psychological issue, like psychosis.
- an eye problem called wide-angle glaucoma.
- surgery on the upper part of your stomach.
- Polyneuropathy or medical condition that is associated with polyneuropathy. Progressive weakness, pain, numbness or loss of sensation in the fingers or feet(symptoms of polyneuropathy) have been reported in patients treated with levodopa/carbidopa intestinal gel. Your doctor will check for the signs and symptoms of polyneuropathy before you start therapy with Lecigon and periodically thereafter.

Contact a doctor immediately if you experience any of the following symptoms during your treatment with Lecigon:

- **Neuroleptic malignant syndrome:**
  A serious condition with a combination of muscle stiffness, cramps, shaking, sweats, fever, rapid pulse, severe blood pressure fluctuations, acting out, confusion, loss of consciousness.
- **Rhabdomyolysis:**
  A serious condition with unexplained muscle pain, muscle cramps or muscle weakness. Rhabdomyolysis can be caused by neuroleptic malignant syndrome.
  → For more information about neuroleptic malignant syndrome and rhabdomyolysis, see section 3 “If you stop or lower your dose of Lecigon” and section 4 “Possible side effects”.
- **Problems from the tube or from the surgery:**
  Stomach pain, nausea or vomiting. This may be due to serious problems caused by the tube or the surgery, e.g. blockage, wound or damage in the intestine.

Talk to your doctor if you experience any of the following **during treatment** with Lecigon:

- You feel **depressed**, have **suicidal thoughts** or if you or other people notice any **mental changes**.
- You notice any **unusual birthmarks** or moles on your skin that suddenly appear or get worse.
- You develop **involuntary movements** (dyskinesia). If you have not been treated with entacapone (one of the active substances in Lecigon) previously, the symptoms may be because entacapone enhances the effects of levodopa and carbidopa (other active substances in Lecigon). The doctor may need to reduce your dose.
- You feel like the **effect of the treatment suddenly or gradually worsens**, e.g. you have difficulty moving/slow movements (bradykinesia). This could be because the tube has slipped out of position in the small intestine or is blocked. It could also be because the pump is not working properly.
- You develop **diarrhoea**. It may be necessary to monitor your weight to avoid any significant weight loss, or it may be necessary to discontinue the treatment. Prolonged or persistent

diarrhoea may be a sign of inflammation in the intestine. In such case, your doctor will need to review your treatment with Lecigon.
- You experience a **loss of appetite** that worsens over time, **a feeling of weakness** and **weight loss** within a short period of time. A general medical examination, including a liver function check, may be required.

If you are unable to handle the pump and tube, you must get help from a caregiver (e.g. nurse, assistant nurse or close relative) to avoid complications (problems).

Impulse control disorders – changes in your behaviour
Tell your doctor if you, your family or carer notices that you are developing urges or cravings to behave in ways that are unusual for you, or you cannot resist the impulse, drive or temptation to perform certain activities that could harm yourself or others. These behaviours are called "impulse control disorders" and can include addictive gambling, excessive eating or spending, abnormally high sex drive or an increase in sexual thoughts or feelings. Your doctor may need to adjust your dose or discontinue your treatment. For more information, see section 4 "Possible side effects".

Dopamine dysregulation syndrome
Tell your doctor if you or your family/carer notices you are developing addiction-like symptoms leading to a craving for larger and larger doses of Lecigon and other medicines used to treat Parkinson's disease.

Regular checks
With long-term treatment with Lecigon, your doctor may need to perform regular checks of your liver and kidney function, blood counts, heart and blood vessels, and examine your skin to detect any skin changes.

Lecigon and cancer
Lecigon contains hydrazine, which forms when carbidopa (an active substance of Lecigon) is broken down. Hydrazine could cause damage to your genes, which could possibly lead to cancer. However, it is not known if the amount of hydrazine produced when taking the recommended dose of Lecigon can cause damage or disease.

Surgery
Before undergoing any operation, including dental surgery, let your doctor or dentist know that you are using Lecigon.

Urine analysis
The active substances levodopa and carbidopa may cause misleading results in urine analyses. Let the healthcare professional know that you are using Lecigon if you are asked to provide a urine sample.

Children and adolescents
Lecigon must not be given to children or adolescents under 18 years of age.

Other medicines and Lecigon
Tell your doctor or pharmacist if you are using, have recently used or might use any other medicines.

Do **not** use Lecigon if you are taking**:**
- Medicines for depression called selective MAO-A inhibitors (like moclobemide) and non-selective MAO inhibitors (like phenelzine). Treatment with these medicines must be discontinued at least two weeks before starting treatment with Lecigon.

Lecigon may enhance the effect and side effects of other medicines and other medicines may enhance the effect and side effects of Lecigon. Let your doctor know if you are taking:

- Medicines for depression called tricyclic medicines (like clomipramine, amitriptyline and nortriptyline). Other types of antidepressant medicines may also affect or be affected by Lecigon.
- Medicines for Parkinson's disease called selective MAO-B inhibitors (like selegiline), amantadine and dopamine agonists (like piribedil) and anticholinergics (like biperide).
- Medicines for urinary incontinence (like oxybutynin), asthma and chronic obstructive pulmonary disease, COPD (like ipratropium and tiotropium). These medicines are known as anticholinergics.
- Some asthma and allergy medicines (like salbutamol and terbutaline) and adrenaline. These medicines are known as sympathicomimetics.
- Medicines to reduce blood pressure (called antihypertensives). Using these and Lecigon at the same time could cause blood pressure drops when you stand up from sitting or lying down. It may be necessary to adjust the dose of your antihypertensive medicine.
- Warfarin (a medicine to prevent blood clots). If you are being treated with Lecigon, or start, end or change your treatment with Lecigon, the effect of Warfarin should be checked.

Some medicines can reduce the effect of Lecigon. Let your doctor know if you are taking:
- Any iron product that is taken by mouth (tablets, capsules, solution). Iron can impair the absorption of levodopa from the gastrointestinal tract (and vice versa). You should therefore take Lecigon and your iron supplement at least 2–3 hours apart. If you do not use your pump at night, you can take the iron supplement before going to bed.
- Medicines for psychosis (like phenothiazines, butyrophenons (e.g. haloperidol) and risperidone).
- Medicines for nausea (like metoclopramide).
- Medicines for epilepsy (like clonazepam and phenytoin).
- Medicines for anxiety and sleeping pills, known as benzodiazepines (like diazepam, oxazepam and nitrazepam).
- Medicines for tuberculosis (isoniazide).
- Medicines for gastrointestinal cramps (papaverine).

Lecigon with food and drink
Lecigon is not absorbed well if taken immediately after eating protein-rich foods (e.g. meat, fish, dairy products, nuts and seeds). Talk to your doctor if you eat a protein-rich diet.

Pregnancy, breastfeeding and fertility
If you are pregnant or breastfeeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

Lecigon is not recommended during pregnancy or to women of childbearing potential not using contraception unless the doctor determines that the benefits for the mother outweigh the possible risks to the foetus.

You should not breastfeed while being treated with Lecigon.

Driving and using machines
Lecigon can have a major influence on the ability to drive and use machines. Do not drive or use machines until you are sure how Lecigon affects you.

- Lecigon may make you feel very sleepy, or you may sometimes find yourself suddenly falling asleep (sleep attacks).
- Lecigon may cause your blood pressure to drop, e.g. when you stand up from sitting or lying down, and make you feel dizzy.

Wait until you feel fully awake again or you no longer feel light-headed or dizzy before driving, using tools or machines, or performing any activities where lack of concentration may put you or others at risk.

Lecigon contains sodium
This medicine contains 166 mg sodium (main component of cooking/table salt) in each cartridge. This is equivalent to 8,3% of the recommended maximum daily dietary intake of sodium.

3. How to use Lecigon

Always use Lecigon exactly as your doctor, nurse or pharmacist has told you. Check with your doctor, nurse or pharmacist if you are not sure.

How Lecigon is given
Lecigon is a gel that travels through a portable pump (Crono LECIG) and tube directly into the upper part of your intestine. The gel is found in the cartridge connected to the pump. The pump is connected to a tube that has been surgically positioned in your intestine via the abdominal wall.

The pump gives you a small dose throughout the day. This means that the level of the medicine in your blood stays the same. It also means that some side effects, like those affecting movement, are lower compared to medicines taken by mouth.

Before the tube is inserted into your small intestine, the doctor may choose to check whether treatment with Lecigon works for you. In such cases, the gel is given via a tube that passes through your nose, throat and stomach to your small intestine.

A manual with instructions for using the pump is supplied with the pump.

Dosage
The doctor adjusts the doses to you individually based on previous medication. It may be necessary to fine-tune the dose during the first few weeks of treatment.

A larger dose (called a bolus dose) is usually given in the morning when treatment is started so the blood reaches the right levels of medicine quickly. After this, a continuous maintenance dose is given during the waking hours (usually about 16 hours). If necessary, your doctor can decide to give Lecigon up to 24 hours a day.

Extra doses can also be given as needed. Some individuals may also need to increase or decrease the continuous maintenance dose during the day. How and when you take the extra doses or adjust the dose during the day will be decided by your doctor after consulting with you.

The total daily dose, including morning dose (bolus dose), maintenance dose and extra doses may not exceed 100 ml (which corresponds to 2000 mg levodopa, 500 mg carbidopa and 2000 mg entacapone).

If the user has dementia, the doctor may decide that the pump may only be handled by a healthcare professional or relative. The pump can be locked to prevent the daily recommended dose from being exceeded accidentally.

Opened cartridge
The cartridge of medicine is for single use only, and must not be used for more than 24 hours, even if there is medicine left. The dosage pump with installed cartridge can be worn close to the body for up to 16 hours. During overnight treatment, the pump should not be worn next to the body but can, for example, be kept on the bedside table. If there was a break in treatment during the night, you can continue using the opened cartridge the next day, but only for up to 24 hours after it was first opened. Do not remove the cartridge from the pump until you are finished using it (i.e. either after 24 hours have passed since it was opened or when it is empty, whichever occurs first).

The gel may become slightly yellow/reddish towards the end of its shelf life. This does not impact the effect of the treatment.

If you use more Lecigon than you should.
Talk to your doctor if you experience any signs of overdose.

Signs of overdose can include:
- Twitching or cramping in your eyelids that make it hard to open your eyes.
- Involuntary, persistent muscle contractions that lead to repeated twisting movement or abnormal body position (dystonia).
- Involuntary movements (dyskinesia).
- Unusually fast, slow or irregular heartbeats.
- Confusion or worry/restlessness.
- Discolouration of the skin, tongue, eyes or urine.

If you forget to use Lecigon
Start the pump as prescribed as soon as possible. Do not increase the dose to compensate for the forgotten dose.

If you stop or lower your dose of Lecigon
Do not stop taking Lecigon or lower your dose without discussing it with your doctor.

This is because suddenly lowering your dose or stopping treatment with Lecigon too quickly could lead to serious conditions called neuroleptic malignant syndrome and rhabdomyolysis. There is a great risk of these conditions occurring if you are being treated with a medicine for a serious psychological issue at the same time. For more information on these conditions, see section 4 “Possible side effects”.

If treatment is discontinued, you will receive another treatment instead. If treatment with Lecigon is being discontinued permanently, the tube will be removed and the wound will be allowed to heal.

If you have any further questions about this medicine, ask your doctor, pharmacist or nurse.

4. Possible side effects

Like all medicines, this medicine may cause side effects, although not everybody gets them. To reduce the risk of side effects, it is important for the dose of the medicine to be adjusted individually with appropriate setting of the pump.

<u>Serious side effects from Lecigon</u>
Contact a doctor immediately if you experience any of the following symptoms during your treatment with Lecigon – you may need urgent medical treatment:

- Itching, hives, swelling of the face, lips, tongue or throat, which may make it difficult to breathe or swallow. Drop in blood pressure. This could be a sign of a severe **allergic reaction** *(rare side effect).*

- A combination of muscle stiffness, cramps, shaking, sweats, fever, rapid pulse, severe blood pressure fluctuations, acting out, confusion, loss of consciousness. These can be symptoms of a serious condition called **neuroleptic malignant syndrome** *(affects an unknown number of users).*

- Unexplained muscle pain, muscle cramps or muscle weakness which may be a sign of **rhabdomyolysis**, a severe, rare muscle disorder with the breakdown of muscle cells that could severely affect the kidneys *(frequency not known (cannot be estimated from data))*. Rhabdomyolysis can be caused by neuroleptic malignant syndrome.

For more information about neuroleptic malignant syndrome and rhabdomyolysis, see section 3 “If you stop or lower your dose of Lecigon”.

- Stomach pain, nausea or vomiting. This may be due to **serious problems caused by the tube or the surgery**, e.g. blockage, wound or damage in the intestine *(common side effect)*.

- Infection with symptoms such as fever with severely impaired general condition or fever with local infection symptoms, such as sore throat/mouth or difficulty urinating. This may be a sign that the white blood cells are affected, a condition called **agranulocytosis** *(frequency not known - cannot be estimated from available data)*. Your doctor will take a blood sample to check this.

- Suicidal thoughts or suicide attempts *(uncommon side effect)*.

Other side effects from Lecigon

Very common (may affect more than 1 in 10 people):
- Weight loss.
- Anxiety, depression, insomnia.
- Involuntary movements (dyskinesia).
- Worsening of Parkinson's disease symptoms.
- Dizziness when you stand up or change positions (orthostatic hypotension) – this is from low blood pressure.
- Nausea, constipation, diarrhoea.
- Pain in muscles, tissues and the skeleton.
- Abnormal urine colour (chromaturia).
- Urinary tract infection.
- Risk of falling.

Common (may affect up to 1 in 10 people):
- Anaemia.
- High levels of amino acids (e.g. homocysteine) in the blood, vitamin B6 and B12 deficiency.
- Loss of appetite, weight gain.
- Nightmares, acting out, restlessness, confusion, hallucinations, psychotic disorders.
- Sleep attacks, sleepiness, sleep disorders.
- Dizziness, fainting, headache.
- Decreased sensation of touch, sense of tingling or numbness in the skin.
- Nerve disorder, with discomfort, pain and tingling, particularly in the feet (polyneuropathy).
- Involuntary, persistent muscle contractions that lead to repeated twisting movement or abnormal body position (dystonia), excessive movements (hyperkinesia), shaking (tremor).
- Changes in the effect on Parkinson's symptoms (On/Off episodes).
- Blurred vision.
- Irregular heartbeat, cardiovascular disease other than heart attack (e.g. angina).
- High or low blood pressure.
- Breathing difficulties, pneumonia due to foreign material in the lungs.
- Pain in the mouth or throat.
- Abdominal distension, abdominal pain, abdominal discomfort, sensitive stomach with pain, heartburn, bloating, vomiting.
- Dry mouth, changed perception of taste.
- Difficulty swallowing, sore throat.
- Contact dermatitis, itching, skin rash.
- Severe sweating.
- Pain, pain in the joints, neck pain, muscle spasms.
- Urinary leakage (urinary incontinence), difficulty urinating.
- Feeling of weakness, fatigue, chest pain.
- Gait disturbance.

- Swelling in the legs or feet.

Impulse control disorders – **changes in your behaviour.** This is a common side effect *(may affect up to 1 in 10 people)*:
Inability to resist the urge to perform an action that may be harmful, including:
- A strong impulse to gamble too much, despite serious effects on you or your family.
- A change or increase in sexual thoughts and behaviour of significant concern to you or to others. This could include an increased sexual drive.
- An uncontrollable and excessive need to buy things and spend money.
- Binge eating (eating large amounts of food in a short time) or compulsive eating (eating more food than normal and more than what you need to satisfy your hunger).

Tell your doctor if you, your family or carer notice any of these behaviours. Your doctor will discuss ways to manage or reduce the symptoms.

Uncommon (may affect up to 1 in 100 people):
- Lower number of white blood cells or platelets in the blood, which may cause bleeding.
- Suicide.
- Confusion, elevated mood (euphoric mood), fear, nightmares.
- Trouble coordinating muscle movements, fits (convulsions).
- Twitching or cramping in your eyelids that make it hard to open your eyes, double vision, optic nerve damage, narrow angle glaucoma (acute elevated pressure in the eye).
- Heart palpitations, heart attack.
- Inflammation in the veins.
- Voice change.
- Inflammation in the large intestines, bleeding in the gastrointestinal tract.
- Abnormally large production of saliva.
- Abnormal liver function test results.
- Skin redness, hives.
- Hair loss, discolouration of nails, skin, hair or sweat.
- Malaise.

Rare (may affect up to 1 in 1000 people):
- Abnormal thoughts.
- Abnormal breathing pattern.
- Grinding of the teeth, pain in the tongue, discoloured saliva.
- Hiccups.
- Skin cancer (malignant melanoma) (see section 2 “Do not use Lecigon”).
- Persistent and painful erection.

Have been reported (affects an unknown number of users):
- Inflammation of the liver (hepatitis).
- Abnormal laboratory results from blood and urine samples.
- Memory impairment, dementia.
- Craving for large doses of Lecigon in excess of that required to control motor symptoms, known as dopamine dysregulation syndrome. Some patients experience severe abnormal involuntary movements (dyskinesias), mood swings or other side effects after taking large doses of Lecigon.

Side effects from the pump, tube or surgery:
Very common (may affect more than 1 in 10 people):
- Abdominal pain
- Infection of the wound after surgery.
- Thick scarring at the site of the incision.
- Problems with tube insertion, such as pain or swelling in the mouth or throat, difficulty swallowing, stomach discomfort, pain or swelling, injury to the throat, mouth or stomach, internal bleeding, vomiting, bloated stomach, anxiety.
- Problems at the site of the incision, redness, sore, stoma leakage, pain or irritation.

Common (may affect up to 1 in 10 people):
- Abdominal discomfort, upper abdominal pain.
- Infection at the surgery site or in the intestine, infection after surgery when the tube was positioned in the intestine.
- Inflammation of the peritoneum (peritonitis).
- The tube changes position from the intestine to e.g. the stomach or is blocked, which can lead to decreased response to treatment.
- Problems in the gastrointestinal tract due to the stoma (where the tube enters the abdomen), pain at the incision, stop of bowel movements after surgery, and problems, discomfort or bleeding as the result of the treatment procedure.

Uncommon (may affect up to 1 in 100 people):
- Inflammation of the large intestine or pancreas.
- Inflammation of the pancreas (pancreatitis).
- The tube penetrates the large intestine wall.
- Blockage in the intestines, bleeding or ulcer in the small intestine.
- Part of the intestine folds into the section next to it (intussusception).
- Blockage of the tube due to undigested food getting stuck around the tube.
- Abscess after insertion of the tube in the intestine.

Have been reported (affects an unknown number of users):
- Reduced blood flow in the small intestine.
- The tube penetrates the stomach wall or small intestine.
- Blood poisoning (sepsis)

Side effects when levodopa and carbidopa are taken by mouth
The following side effects have been reported with levodopa and carbidopa (the same active substances as in Lecigon) when taken by mouth. These side effects could also occur with Lecigon.

Rare (may affect up to 1 in 1000 people):
- Anaemia due to increased breakdown of red blood cells.
- Inability to open the mouth all the way.
- Symptoms from one half of the face, including hanging eyelids (Horner's syndrome).
- Widening of the pupil in the eye, convulsive movement of the eyeballs to a fixed position, usually upwards.
- Inflammation of the small blood cells causing, among other things, raised bruises (Henoch-Schönlein purpura).

Very rare (may affect up to 1 in 10,000 people):
- Changed blood counts.

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the Yellow Card Scheme, Website: www.mhra.gov.uk/yellowcard
or search for MHRA Yellow Card in the Google Play or Apple App Store.

By reporting side effects, you can help provide more information on the safety of this medicine.

5. How to store Lecigon

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the label and carton after EXP.

Unopened cartridge: Store in a refrigerator (2°C–8°C). Do not freeze.
Store in the original packaging in order to protect from light.

Opened cartridge: Use immediately. The product can be used for up to 24 hours after being removed from the refrigerator. The dosing pump with installed cartridge can be worn close to the body for up to 16 hours. During overnight treatment, the pump should not be worn next to the body but can, for example, be kept on the bedside table. Discard any unused amount after 24 hours.

The cartridges are intended for single use only. Do not reuse an opened cartridge.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Lecigon contains
- The active substances are levodopa, carbidopa monohydrate and entacapone. 1 ml contains 20 mg levodopa, 5 mg carbidopa monohydrate and 20 mg entacapone.
- The other ingredients are carmellose sodium, hydrochloric acid (for pH adjustment), sodium hydroxide (for pH adjustment), and water.

What Lecigon looks like and contents of the pack
Lecigon intestinal gel is a yellow or yellowish-red opaque viscous gel.
The container is a plastic cartridge containing 47 ml of intestinal gel.

One pack contains 7 cartridges.

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