

PATIENT PACKAGE INSERT IN ACCORDANCE WITH THE PHARMACISTS' REGULATIONS (PREPARATIONS) - 1986
The medicine is dispensed with a doctor's prescription only

DUODOPA

Gel for a continuous infusion directly into the digestive system with the help of a designated device

Active ingredients:

Levodopa 20 mg/ml

Carbidopa (as monohydrate) 5 mg/ml

Inactive ingredients: See section 6 'Further Information'.

Read this leaflet carefully in its entirety before using the medicine. This leaflet contains concise information about the medicine. If you have further questions, refer to the doctor or pharmacist.

This medicine has been prescribed for the treatment of your ailment. Do not pass it on to others. It may harm them even if it seems to you that their ailment is similar.

The medicine is not intended for children and adolescents below the age of 18.

In addition to the leaflet, Duodopa has a patient safety information card. This card contains important safety information, which you should know before starting and during the treatment with Duodopa and act accordingly. Read the patient safety information card and the patient leaflet before start using the preparation. Keep the card for further reference if needed.

1. WHAT IS THE MEDICINE INTENDED FOR?

Duodopa is intended for the treatment of advanced levodopa-responsive Parkinson's disease accompanied by severe motor fluctuations and hyper-/dyskinesia when available combinations of medicinal products for the treatment of Parkinson's have not given satisfactory results.

Therapeutic group: anti-Parkinson's components
Levodopa – a dopamine derivative
Carbidopa (as monohydrate) – dopa-decarboxylase enzyme inhibitor

Duodopa belongs to a group of medicines to treat Parkinson's disease. It is a gel that goes through a pump and a tube into your gut (small intestine).

Duodopa contains two active substances: levodopa and carbidopa (as monohydrate).

How the medicine works:

- In the body, levodopa is made into “dopamine”. This adds to the dopamine already in your brain and spinal cord. Dopamine helps transfer signals between nerve cells.
- Too little dopamine causes Parkinson's disease signs like tremor, feeling stiff, slow movement, and problems keeping your balance.
- Treatment with levodopa increases the amount of dopamine in your body. This means it reduces these signs.
- The role of carbidopa (as monohydrate) is to improve the effect of levodopa and reduce the side effects of levodopa.

2. BEFORE USING THE MEDICINE

2.1 Do not use the medicine if:

- You are sensitive (allergic) to levodopa, carbidopa or any of the other ingredients contained in the medicine (see section 6 'Further Information').
- You have an eye problem called 'narrow-angle glaucoma'.
- You have severe heart problems.
- You have a severe uneven heart beat (arrhythmia).
- You have had a severe stroke.
- You are taking certain medicines for depression [medicines from the non-selective MAO (monoamine oxidase) inhibitors or selective MAO-A inhibitors group, such as: moclobemide or phenelzine].
- You have a tumor of the adrenal gland (pheochromocytoma).
- You have hormone problems such as overproduction of cortisol (Cushing's syndrome) or of thyroid hormones (hyperthyroidism).
- You have ever had skin cancer, or you have any unusual moles or marks on your skin which have not been looked at by the doctor.

Do not use Duodopa if any of the above apply to you. If you are not sure, talk to a doctor before having Duodopa.

2.2 Special warnings regarding use of the medicine:

■ Before treatment with Duodopa, tell the doctor if:

- You have ever had a heart attack, blocked blood vessels in your heart or suffered from any other heart problems including an uneven heart beat (arrhythmia).
- You have a lung problem – e.g., asthma.
- You have ever had a hormone problem.
- You have ever had depression with suicidal tendencies or from any other mental problem.
- You have an eye disease called 'wide-angle glaucoma'.
- You have ever had a stomach ulcer.
- You have ever had fits (convulsions).
- You have ever had surgery in your upper stomach area (upper abdominal surgery).

Progressive weakness, pain, numbness or loss of sensation in the fingers or in the feet (polyneuropathy) have been reported in patients treated with levodopa/carbidopa intestinal gel. Your doctor will check for the signs and symptoms of neuropathy before you start levodopa/carbidopa intestinal gel and periodically thereafter. Tell your doctor if you already have neuropathy or a medical condition that is associated with neuropathy.

If any of the above apply to you (or you are not sure), talk to a doctor before using the medicine.

■ It is important to be aware of the following information and side effects that can develop with use of Duodopa:

Neuroleptic Malignant Syndrome:

Do not stop having Duodopa or lower your dose unless a doctor tells you to. This is because suddenly stopping or lowering your Duodopa dose quickly may cause a serious problem called: “Neuroleptic Malignant Syndrome” (see section 3 'How should you use the medicine?' and section 4 'Side Effects').

Feeling sleepy and dizzy:

If you suddenly fall asleep (sleep attacks), or feel very sleepy, or if you feel light-headed or dizzy:

- Do not drive or use any tools or machines until you feel fully awake again or you no longer feel light-headed or dizzy (see section 'Driving and using machines').

Skin changes:

Tell the doctor if you notice any unusual marks or moles on the skin that appear or get worse (see section 4 'Side Effects').

Impulse control disorders – changes in your behavior:

Tell your doctor if you, your family or carer notice you are developing urges or cravings to behave in ways that are unusual for you or if you cannot resist the impulse, drive or temptation to carry out certain activities that could harm yourself or others. These behaviors are called “impulse control disorders” and can include:

- addictive gambling
- excessive eating or spending
- increased sex drive or an increase in sexual thoughts or feelings

Your doctor may need to review the treatments you are receiving. The doctor will discuss with you ways of controlling or reducing these symptoms (see section 4 'Side Effects').

Dopamine Dysregulation Syndrome:

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

Problems using the pump or tube:

There may be some problems linked to using the pump and tube:

- You become less able to handle the pump and tube, your Parkinson's disease symptoms get worse or it is harder for you to move (bradykinesia) – these effects may indicate that the pump and tube are not working properly.
- If you have pain in the stomach area, you feel nauseous and vomit – refer to the doctor immediately (see section 4 'Side Effects').
- You may get other side effects affecting your intestine and where the tube goes in (see section 4 'Side Effects').

Duodopa and cancer:

In the body, carbidopa (one of the active ingredients in Duodopa) is broken down to a substance called hydrazine. This substance may cause damage to your genetic material, which could lead to cancer. However, it is not known if the amount of hydrazine produced when taking a normal dose of Duodopa can cause this.

Children and adolescents:

Do not give Duodopa to children and adolescents under the age of 18 years.

Tests and follow-up:

Your doctor may do some blood tests if you are having this medicine.

Operations:

Before you have an operation (including a dental operation), tell the doctor (or dentist) that you are having Duodopa.

2.3 Drug Interactions

If you are taking, or if you have recently taken, other medicines, including non-prescription medicines and nutritional supplements, tell the doctor or pharmacist.

Do not use Duodopa if you are taking antidepressants of the selective MAO-A enzyme inhibitors or nonselective MAO inhibitors, such as moclobemide or phenelzine.

Before beginning treatment with Duodopa, inform the doctor or pharmacist if you are taking other medicines for the treatment of:

- Anemia – such as: iron tablets.
- Tuberculosis – such as: isoniazid.
- Anxiety – such as: benzodiazepines.
- Sickness – such as: metoclopramide.
- High blood pressure – such as: anti-hypertensives.
- Spasms in the blood vessels – such as: papaverine.
- Fits (convulsions) or epilepsy – such as: phenytoin.
- Parkinson's disease – such as: tolcapone, entacapone, amantadine.
- Mental problems – such as: anti-psychotics including: phenothiazines, butyrophenones and risperidone.
- Severe allergic reactions, asthma, chronic bronchitis, heart diseases and low blood pressure – such as anti-cholinergics and sympathomimetics.
- You are taking a medicine which may cause low blood pressure. This could cause something called 'orthostatic hypotension' – this can make you dizzy when getting up from a chair or bed. Duodopa can make this worse. Always change positions slowly.

2.4 Use of Duodopa with food and drink:

For some patients, Duodopa may not work well if it is taken with, or shortly after eating protein-rich food – such as meat, fish, dairy products, seeds and nuts. Talk to your doctor if you think this applies to you.

2.5 Pregnancy and breastfeeding:

- Consult your doctor before starting treatment with Duodopa, if you are pregnant or breastfeeding, think you may be pregnant or are planning to become pregnant.
- Do not use Duodopa if you are breastfeeding.

2.6 Driving and use of machines:

Do not drive or use tools or machines until you are sure how Duodopa affects you.

- Duodopa may make you feel very sleepy, or you may sometimes find yourself suddenly falling asleep (sleep attacks).
- Duodopa may lower your blood pressure, which can make you feel light-headed or dizzy.

Do not drive or use any tools or machines until you feel fully awake again or you no longer feel light-headed or dizzy.

3. HOW SHOULD YOU USE THE MEDICINE?

- Always use the medicine according to doctor's instructions.
- The dosage and treatment regimen will be determined by the doctor only.
- Check with the doctor or pharmacist if you are not sure regarding the dosage and the treatment regimen of the medicine.

Information about Duodopa gel and the pump

- Duodopa is a gel that goes through a pump and a tube into your gut (small intestine).
- The gel comes in a plastic cassette. The cassette is connected to a pump.
- The pump is connected to a tube which is placed into your gut (small intestine).
- You are given a small dose throughout the day. This means that the level of the medicine in your blood stays the same. It also means some of the movement side effects are lower.

The dosage of Duodopa that is given

- Your doctor will decide how much Duodopa you should use and for how long.
- Usually, a larger morning dose (bolus dose) is given. This allows you to quickly get the right amount of medicine in your blood. After that dose, a steady ('maintenance') dose is given.
- If needed, you may have extra doses – this will be decided by your doctor.

- **Do not exceed the recommended dose.**

If you have taken a higher dosage

If you accidentally took too high a dosage of Duodopa or took an overdose, or if a child has accidentally swallowed the medicine, refer immediately to a doctor or proceed to a hospital emergency room, and bring the package of the medicine with you.

In such cases, the following effects may occur:

- Problems opening your eyes.
- Muscle spasms you cannot control in your eyes, head, neck and body (dystonia).
- Movement you make without wanting to (dyskinesia).
- Unusually fast, slow or uneven heart beats (arrhythmia).

If you forgot to take Duodopa

- Start your pump, with your normal dose, as soon as possible.
- Do not increase your dose to make up for a forgotten dose.

If you stopped taking Duodopa or lowered the dosage

Do not stop the treatment or lower the dosage of Duodopa, unless the doctor tells you to, this is because suddenly stopping or lowering your Duodopa dose quickly may cause a serious problem called “Neuroleptic Malignant Syndrome”.

This problem is more likely to happen if you are also taking a anti-psychotic medicine (see section 4 'Severe side effects').

Adhere to the treatment as recommended by the doctor.

Even if there is an improvement in your health, do not stop treatment with the medicine without consulting the doctor or pharmacist.

Do not take medicines in the dark! Check the label and the dose each time you take medicine. Wear glasses if you need them.

If you have further questions regarding use of the medicine, consult a doctor or pharmacist.

4. SIDE EFFECTS

As with any medicine, use of Duodopa may cause side effects in some users. Do not be alarmed when reading the list of side effects. You may not suffer from any of them.

Severe side effects from use of Duodopa:

Stop using the medicine and refer to the doctor immediately if you notice any of the following side effects - you may need urgent medical treatment:

- Acute pain in eyes, headache, blurred vision, nausea and vomiting. These may be signs of angle closure glaucoma. This adverse event is uncommon (effect that occurs in 1-10 out of 1,000 users).
- Fever, sore throat or mouth, or trouble passing water. These may be signs of a white blood cell problem called 'agranulocytosis'. Your doctor will take a blood sample to check for this. The frequency of this effect is very rare (effect that occurs in less than 1 out of 10,000 users).
- Swelling of the face, tongue or throat, which may make it difficult to swallow or breathe, or nettle type skin rash. These may be signs of a severe allergic reaction ('anaphylactic reaction'). The frequency of this effect is not known from available data.

Tell your doctor straight away if you notice any of the following serious side effects:

- 'Neuroleptic Malignant Syndrome' – the signs of this effect may include:
 - Fast heartbeat, changing blood pressure and sweating, followed by fever.
 - Faster breathing, muscle stiffness, lower consciousness and coma.
 - Higher levels of a protein in your blood (an enzyme called 'creatine phosphokinase'). This is measured by your doctor. The frequency of this effect is rare (effect that occurs in 1-10 out of 10,000 users).
- See section 3 'How should you use the medicine?' and section 2.2 'Special warnings regarding use of the medicine:'.

Other side effects from use of Duodopa:

Tell the doctor if you notice any of the following side effects:

Very common side effects (effects that occur in more than 1 in 10 users):

- Falling
- Weight loss
- Nausea, constipation
- Anxiety, depression, not being able to sleep (insomnia)
- Movement you make without wanting to (dyskinesia), worsening of Parkinson's disease symptoms
- Feeling dizzy when you stand up or change positions ('orthostatic hypotension'), this is from low blood pressure. Always change positions slowly – do not stand up quickly.

Common side effects (effects that occur in 1-10 out of 100 users):

- Weight gain
- Uneven heartbeat
- Not wanting to eat
- Feeling tired, weak
- High or low blood pressure
- Anemia – low levels of iron in the blood
- Pain, neck pain, muscle cramps, muscle weakness
- Suddenly falling asleep (sleep attacks), feeling very sleepy, sleep disorders
- Higher levels of amino acids or homocysteine in the blood, having too little vitamin B6 and B12
- A feeling of dizziness/feeling like you are going to faint, or fainting (syncope)
- Difficulty swallowing or dry mouth, change in taste (bitter taste in the mouth)
- Headache
- Progressive weakness or pain or numbness or loss of sensation in the fingers or feet (polyneuropathy)
- Rashes, itching, increased sweating, swelling caused by too much fluid (oedema)
- Difficulty passing water (retention of urine) or unable to control water flow (incontinence)
- Seeing, hearing or feeling things that are not there (hallucinations), confusion, abnormal dreams, agitation, impulsive behavior, psychotic disorder
- Having a swollen stomach, diarrhea, wind (flatulence), indigestion (dyspepsia), vomiting
- Parkinson's disease symptoms coming back quickly or when not expected – this is called the 'on and off phenomenon'
- Reduced sense of touch, muscle spasms you cannot control – affecting your eyes, head, neck and body (dystonia), shaking

Impulse control disorders – changes in your behavior. These effects are common, that may affect up to 1 in 10 people.

Some people are unable to resist the impulse to do something that could be harmful to themselves or others. This may include:

- A strong impulse to gamble too much, despite serious effects on you or your family.
- A change or increase in sexual thoughts and behavior, of significant concern to you or to others, that could include an increased sexual drive.
- Excessive, uncontrollable shopping or spending.
- Binge eating – eating large amounts of food in a short time, or compulsive eating – eating more food than normal and more than your body needs.

Tell your doctor if you, your family or carer notice any of these behaviors. Your doctor may need to review your treatment and will discuss ways of treating or reducing these symptoms with you.

Uncommon side effects (effects that occur in 1-10 out of 1,000 users):

- Dark urine
- Hoarseness, chest pain
- Hair loss, red skin, hives
- Having more saliva than usual
- Swelling in the veins (phlebitis)
- A change in the way you walk
- Suicide attempt
- Feeling tired or generally unwell
- Fast and uneven beats of the heart (palpitations)
- Low number of white blood cells or changes in blood cell counts which may cause bleeding
- Confusion, euphoric mood (abnormally elevated mood), increased sexual interest, nightmares, dementia, feeling of fear
- Problems controlling movements, and making strong movements you cannot control
- Problems opening your eyes, double vision, blurred vision, optic nerve damage (optic ischaemic neuropathy)

Rare side effects (effects that occur in 1-10 out of 10,000 users):

- Abnormal thinking
- Uneven breathing pattern
- Painful erection that will not go away
- Unusual marks or moles on your skin that appear or get worse, or tumor of the skin (malignant melanoma)
- Dark saliva or sweat, burning feeling on the tongue, grinding of your teeth, hiccups

Side effects of unknown frequency (effects whose frequency has not yet been determined):

- Craving for large doses of Duodopa 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 Duodopa.

Tell the doctor if you notice any of the side effects mentioned above.

Side effects from use of the pump or tube:

The following side effects have been reported for the pump and tube.

Refer to a doctor or nurse if you experience any of these effects.

- If you become less able to handle the pump and tube, if your Parkinson's disease symptoms get worse or if it is harder for you to move (bradykinesia) – these effects may indicate that the pump and tube are not working properly.
- If you have pain in the stomach area, you feel nauseous and vomit - refer to the doctor immediately, you might have a problem with the pump or tube.

Very common side effects (effects that occur in more than 1 in 10 users):

- Stomach pain
- Infection where the tube goes into your stomach – caused by the surgery
- Thick scarring where the tube goes into your stomach
- Problems from having the tube put in – pain or swelling in the mouth or throat, difficulty swallowing, stomach discomfort, pain or swelling, injury to the throat, mouth or stomach, bleeding, vomiting, wind (flatulence), anxiety
- Problems around where the tube goes into the stomach, red or injured skin, sores, discharge, pain or irritation

Common side effects (effects that occur in 1-10 out of 100 users):

- Incision site infection, infection after the tube is placed in the intestine
- Inflamed wall of stomach
- Inflammation in the intestine or where the tube goes into your stomach
- The tube moves around in the gut or gets blocked – which could cause lower amounts of medicine to be absorbed
- Pain when breathing, feeling short of breath, chest infections (pneumonia, including aspiration pneumonia)

Uncommon side effects (effects that occur in 1-10 out of 1,000 users):

- Inflamed colon (colitis)
- Inflamed pancreas
- The tube goes through the wall of the large intestine
- Blockage (obstruction), bleeding or ulcer in the gut
- Sliding of one part of the gut into an adjacent part of the gut (intussusception)
- Food getting stuck around the tube causing it to block
- Pocket of infection (abscess) – this could happen after the tube is placed in your stomach

Side effects of unknown frequency (effects whose frequency has not yet been determined):

- Reduced blood flow in the small intestine
- The tube goes through the wall of the stomach or small intestine
- Infection in the blood (sepsis)

The following side effects have been observed with medicines that contain levodopa/carbidopa taken by mouth:

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

Rare side effects (effects that occur in 1-10 out of 10,000 people):

- Anemia – low levels of iron in the blood
- An eye problem called Horner's syndrome
- Not being able to open your mouth all the way (trismus)
- Red or purple skin rash that looks like small blisters (Henoch-Schönlein Purpura)
- Neuroleptic malignant syndrome (see section 3 'How should you use the medicine?' and section 4 'Side Effects')
- Widening of the pupil in your eye for a long period of time (mydriasis), decreased eye movement

Very rare side effects (effects that occur in less than 1 out of 10,000 people):

- Changes in blood test values

Reporting side effects

Side effects can be reported to the Ministry of Health by clicking on the link “Report Side Effects of Drug Treatment” found on the Ministry of Health homepage (www.health.gov.il) that directs you to the online form for reporting side effects, or by entering the link:

<https://sideeffects.health.gov.il>

If a side effect occurs, if any of the side effects worsen, or when you suffer from a side effect not mentioned in the leaflet, consult with the doctor.

5. HOW SHOULD THE MEDICINE BE STORED?

- Avoid poisoning! This medicine, and any other medicine, should be kept in a closed place out of the reach and sight of children and/or infants in order to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by the doctor.
- Do not use the medicine after the expiry date (exp. date) which is stated on the outer carton package.
- Store in a refrigerator, at a temperature of 2°C-8°C (the temperature range prevailing in most household refrigerators). The drug cassette can be used for up to 24 hours after being taken out of the refrigerator. Use immediately after opening. Discard leftover medicine.
- Keep the cassette in its original carton package in order to protect from light.
- The drug cassettes are intended for single-use only and should not be used for longer than 24 hours, even if a bit of gel remains.
- The gel might become slightly yellow. This has no effect on the medicine.
- Do not re-use an opened cassette.
- Medicines should not be disposed of via wastewater or household waste. Ask the pharmacist how to dispose of medicines that you no longer need. Taking these measures will help to protect the environment.
- Do not re-use used cassettes.

6. FURTHER INFORMATION

- In addition to the active ingredients, the medicine also contains carmellose sodium and distilled water.

What the medicine looks like and the contents of the package:

Duodopa is provided in cassettes (PVC bags protected by hard plastic) containing 100 ml. Each package contains seven cassettes. The gel color is off-white to light yellow.

- **License holder and its address:** Abbvie Deutschland GmbH & CO.KG, Ludwigshafen, Germany.

- **Manufacturer and its address:** Abbvie Deutschland GmbH & CO.KG, Ludwigshafen, Germany.

- Revised in December 2020 according to MoH guidelines.

- **Registration number of the medicine in the National Drug Registry of the Ministry of Health:** 143-32-32029.