

PACKAGE LEAFLET: INFORMATION FOR THE USER

Apodespan PR 50 mg/200 mg Prolonged release tablets Carbidopa and Levodopa

- Read all of this leaflet carefully before you start taking 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 sign 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 Apodespan PR are and what it is used for**
2. **What you need to know before you take Apodespan PR**
3. **How to take Apodespan PR**
4. **Possible side effects**
5. **How to store Apodespan PR**
6. **Contents of the pack and other information**

1. **What Apodespan PR are and what it is used for**

Apodespan PR are used in the treatment of Parkinson's disease. It reduces the "off" time (a sudden onset of muscle stiffness that can last for minutes or even hours) if you are being treated with levodopa alone, levodopa/decarboxylase inhibitor tablets with an immediate-release formulation (e.g. carbidopa) and if you suffer from sudden uncontrolled movements.

Apodespan PR belongs to a class of drugs used to treat Parkinson's disease. The symptoms of this disease are probably caused by a lack of dopamine, a substance that is normally produced by the brain. Dopamine plays a role in controlling muscle movement. A lack of it causes problems in muscle movement. Levodopa compensates for the lack of dopamine, whilst carbidopa ensures that enough levodopa reaches the brain.

2. **What you need to know before you take Apodespan PR**

Do not take Apodespan PR:

- if you are **allergic** (hypersensitive) to **carbidopa or levodopa** or any of the other ingredients of Apodespan PR
- if you have **increased eye pressure** (narrow-angle glaucoma)
- if you are suffering from **severe heart failure**
- if you have a **serious heart rhythm disorder**
- if in the event of a **sudden stroke**
- if you are not allowed to use **drugs that act on the central nervous system** (sympathomimetic agents)
- if you are **using non-selective monoamine oxidase inhibitors and selective, type-A MAO inhibitors** (MAO inhibitors; drugs used in depression). You must stop taking these drugs for at least two weeks before starting treatment with Apodespan PR .
- Apodespan PR may be co-administered with the recommended dose of a MAO inhibitor which is selective for MAO type B (e.g. selegiline). Because levodopa may activate a malignant melanoma,

Carbidopa-levodopa should not be used in patients with suspicious undiagnosed skin lesions or a history of melanoma.

Take special care with Apodespan PR

If you are currently being, or have ever been, treated with levodopa on its own. You must wait for at least 12 hours before you can start taking Apodespan PR

- if you suffer from movement disorders such as facial muscle twitches, muscle rigidity and stiffness, difficulties in starting to move, trembling of the fingers or hands. It may be necessary to reduce the dose.
- if you have ever suffered from involuntary movements in the past
- if you have ever had a psychotic episode or suffered from psychosis. Psychosis is a severe mental illness whereby control over one's own conduct and behaviour is impaired. Very rarely, there have been reports of patients who became depressed and who later developed suicidal tendencies. If you think that this also applies to you, you are advised to contact your doctor immediately.
- if you are constantly tired and/or prone to falling asleep without warning. You must not drive or operate machines; your doctor will adjust your dose if necessary, or stop your treatment altogether.
- if you have a severe cardiovascular condition
- if you have a severe lung disease or if you experience sudden attacks of breathlessness caused by muscular spasms and swelling of the mucous membrane inside the airways, often accompanied by coughing and the production of phlegm (bronchial asthma)
- if you have a kidney or liver disorder, or if you have problems with your endocrine system (glands that secrete hormones internally into the blood stream)
- if you have ever had stomach or intestinal ulcers, as there is a greater risk of stomach bleeding
 - if you are vomiting blood
 - if you have ever had seizures/ convulsions
 - if you have recently had a heart attack and are still suffering from heart rhythm disorders
 - if you have chronic glaucoma (increased eye pressure)
- if your levodopa/carbidopa dose is suddenly lowered or stopped, particularly if you are receiving drugs to treat psychosis; as this may trigger off a change in your mental condition; muscle rigidity and increased body temperature may occur
- if you have an hereditary disease characterised by sudden involuntary but coordinated movements (Huntington's chorea). Use of Apodespan PR is not recommended.
- if you have ever had a malignant melanoma
- if you have a skin condition that has not yet been diagnosed by your doctor
- Apodespan PR could give rise to abnormalities in several laboratory tests. These include:
 - - liver function tests
 - - a false positive coombs test
 - - decreased haemoglobin and haematocrit, elevated serum glucose and white blood cells, bacteria and blood in the urine
- when a test strip is used to determine ketonuria a false positive result for urinary ketone bodies can be shown. This reaction is not altered by boiling the urine sample.
- false negative results can also occur in the examination of glycosuria with the use of glucose oxidase methods
- the safety and efficacy of Apodespan PR in newly-born infants and children under the age of 18 has not been established; the use of Apodespan PR in patients under the age of 18 is therefore not recommended
- pathologically driven gambling and obsessive increased sexual desire have been reported in patients treated for Parkinson's disease with drugs belonging to the group of dopamine agonists, including Apodespan PR.

Please tell your doctor if any one of the above-mentioned warnings applies to you, or has ever applied to you in the past.

Tell your doctor if you or your family/carer notices 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 carry out certain

activities that could harm yourself or others. These behaviours are called impulse control disorders and can include addictive gambling, excessive eating or spending, an abnormally high sex drive or an increase in sexual thoughts or feelings. Your doctor may need to review your treatments.

Taking Apodespan PR with other medicines

Apodespan PR may interfere with the effects/side effects of other drugs, and vice versa. This is particularly true in the case of:

- drugs used to treat high blood pressure; your doctor will need to adjust the dosage
- drugs used to treat depression (see also section "Do not take Levodopa/Carbidopa")
- drugs that act on the central nervous system (anticholinergics; bronchodilators used in asthma), such as ipratropium and tiotropium. The effect of levodopa may be reduced; your doctor will adjust the dosage if necessary
- drugs used to treat psychosis
- isoniazid (a drug used to treat tuberculosis)
- benzodiazepines (certain sleeping pills and tranquilisers), such as diazepam, oxazepam and lorazepam; the effect of Apodespan PR may be reduced
- Phenytoin (a drug used in epilepsy); the effect of Apodespan PR may be reduced
- Papaverine (a drug used to treat spasms in the gastrointestinal tract); the effect of Apodespan PR may be reduced
- selegiline (a drug used in Parkinson's disease); when used at the same time as Apodespan PR, severe low blood pressure may occur
- COMT inhibitors (used in Parkinson's disease); when used at the same time as Apodespan PR, the levels of levodopa reaching the brain may increase. The Levodopa/Carbidopa dose may need to be adjusted.
- amantadine (used in Parkinson's disease). The side effects of levodopa may increase. The Levodopa/Carbidopa dose may need to be adjusted.
- metoclopramide (a gastrointestinal drug)
- drugs that act on the central nervous system (sympathomimetics; bronchodilators used in asthma), such as apraclonidine, dipivefrin and brimonidine. Cardiovascular-related side effects may increase.
- ferrous sulphate. Levodopa absorption may decrease.

Please tell your doctor or pharmacist if you are taking, or have recently taken, any other medicines, including medicines obtained without a prescription.

Taking Apodespan PR with food and drink

The effect of levodopa can sometimes be impaired in patients on a high-protein diet.

Pregnancy and breast-feeding

Ask your doctor or pharmacist for advice before taking any medicine.

- Any woman of childbearing potential who is receiving Apodespan PR 50/200 mg must practise effective contraception.
- Not enough is known about the use of Apodespan PR during human pregnancies. It was shown to be harmful in animal experiments. It is not known whether carbidopa is excreted in human milk.
- Do not take Apodespan PR if you are pregnant, or trying to conceive.
- Levodopa is excreted into breast milk.

You must therefore not breastfeed during treatment with Apodespan PR.

Driving and using machines

Apodespan PR cause side effects such as

- dizziness,
- drowsiness,

- double vision,
which may affect your ability to react.
You should bear this in mind if you intend driving or using machines. Patients who are known to be prone to drowsiness and falling asleep without warning may not drive or use machines.

Apodespan PR contains lactose monohydrate

This medicine contains lactose. If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicine.

3. How to take Apodespan PR

Dosage

Adults and the elderly

Your doctor has prescribed how much Apodespan PR you should take.
Generally speaking, the following doses apply:

If you have never been treated with levodopa:

Starting dose

1 Apodespan PR 50/200 mg twice daily.

Maximum starting dose

3 tablets of 1 Apodespan PR 50/200 mg daily (600 mg of levodopa per day).

Doses should be taken at intervals of at least 6 hours.

If you are switching from normal Levodopa/Carbidopa tablets to prolonged release tablets:

Such a switch should take place gradually and under the supervision of a doctor.

If you are currently being treated with levodopa alone (i.e. on its own):

Treatment with levodopa should be stopped for at least 12 hours before using Apodespan PR.

Starting dose in patients with a mild-to-moderate form of Parkinson's disease:

1 Apodespan PR 50/200 mg twice daily

Maintenance dose:

Your doctor will monitor you on a regular basis and adjust your dosage if necessary.

An interval of at least three days should be allowed between each dose adjustment.

Swallow the tablet whole with a glass of water irrespective of meals, do not break or chew the tablet.

If you have the impression that the effect of Apodespan PR is too strong or too weak, talk to your doctor or pharmacist.

Children and adolescents (under 18 years of age)

The use of Apodespan PR in patients under the age of 18 is not recommended (see section "Take special care with Apodespan PR")

Length of treatment

Your doctor will tell you how long you must keep using Apodespan PR. Do not stop treatment before you should; otherwise, your symptoms may return.

If you take more Apodespan PR than you should

If you have taken too much Apodespan PR contact your doctor or pharmacist immediately.

Overdose symptoms may include: spasms of the orbicularis oculi muscle surrounding the eye (see also section 4. "Possible side effects").

If you forget to take Apodespan PR

Do not take a double dose of Apodespan PR to make up for a forgotten dose. If you have forgotten a dose, you can still take it unless it is almost time for your next dose. If this occurs, continue on your normal dosage schedule.

If you stop taking Apodespan PR

Your doctor will monitor you regularly if your dosage is suddenly lowered or if your treatment is stopped. Please read the section: "Take special care with Apodespan PR", particularly if you are using drugs in the treatment of psychosis (antipsychotic agents).

If you have any further questions on the use of this product, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, Apodespan PR can cause side effects, although not everybody gets them.

Side effects that may occur are:

- very common* in more than one in 10 patients
- common* in more than one in 100 patients, but less than one in 10 patients
- uncommon* in more than one in 1,000 patients, but less than one in 100 patients
- rare* in more than one in 10,000 patients, but less than one in 1,000 patients
- very rare* in less than one in 10,000 patients

Blood and lymphatic system disorders

Rare:

- a blood disorder (lack of white blood cells) accompanied by an increased susceptibility to infections (leukopenia)
- anaemia (haemolytic and non-haemolytic)
- a blood disorder (lack of blood platelets) accompanied by bruising and a tendency to bleed (thrombocytopenia)

Very rare:

- a very serious blood disorder (lack of white blood cells) accompanied by sudden high fever, severe sore throat and mouth ulcers (agranulocytosis).

Metabolism and nutrition disorders

Common:

- loss of appetite (anorexia)

Uncommon:

- weight loss
- weight gain.

Psychiatric disorders

Common:

- seeing things that are not there (hallucinations)
- confusion
- dizziness
- nightmares
- drowsiness
- tiredness
- sleeplessness
- depression with (very rarely) suicidal tendencies
- feeling of well-being (euphoria)
- dementia

- episodes of serious mental illness, during which control over one's own conduct and behaviour is impaired (psychotic episodes including delusions and paranoid ideation)
- feeling of stimulation
- dream abnormalities

Rare:

- excitement (agitation)
- anxiety
- impaired ability to think
- disorientation
- headache
- increased sexual desire
- numbness
- fits/ seizures.

Not Known:

- It was reported that patients treated for Parkinson's disease with drugs belonging to the group of dopamine agonists, including Apodspan PR, have shown signs of pathologically driven gambling and obsessive increased sexual desire, especially at high doses. These side effects generally disappeared upon reduction of the dose or treatment discontinuation.

Nervous system disorders

Common:

- movement disorders (dyskinesia)
- a disorder characterised by sudden involuntary movements (chorea)
- muscle tone disorder (dystonia)
- movement disorders caused from outside the nervous system (extrapyramidal)
- sudden changes in Parkinson's symptoms ("on-off" symptoms)
- slowdown in movements during "on-off" periods (bradykinesia)

Uncommon:

- ataxia
- increase in hand tremors

Rare:

- a serious condition as a result of using neuroleptics, which may manifest as muscle stiffness, a severe inability to sit still, high fever, sweating, increased salivation and impaired consciousness (neuroleptic malignant syndrome)
- feelings of prickling, tingling and itchiness without any apparent cause (paraesthesia)
- fits
- gait disorders
- lockjaw.
- increased libido

Not known:

- Drowsiness and (very rarely) constant daytime fatigue/ sudden attacks of sleep.
- muscle twitching

Eyes disorders

Rare:

- blurred vision
- spasm of the orbicularis oculi muscle surrounding the eye (this may be a sign of overdose)
- activation of a pre-existing Horner's syndrome (an eye disorder)
- double vision
- dilated pupils
- a deterioration in eye movements.

Cardiac (heart) disorders

Common:

- palpitations
- irregular heartbeat.

Vascular disorders

Common:

- a drop in blood pressure caused e.g. by getting up too quickly from a sitting or lying position, sometimes accompanied by dizziness (orthostatic hypotension)
- tendency to faint
- sudden loss of consciousness

Uncommon:

- increase in blood pressure

Rare:

- inflammation of the veins (phlebitis).

Respiratory, thoracic (chest) and mediastinal disorders (i.e. the area between the lungs)

Uncommon:

- hoarseness
- chest pain

Rare:

- breathlessness
- abnormal breathing patterns.

Gastrointestinal disorders

Common:

- nausea
- vomiting
- dry mouth
- bitter taste

Uncommon:

- constipation
- diarrhoea
- increased salivation
- difficulties in swallowing (dysphagia)
- wind

Rare:

- impaired digestion with symptoms such as feelings of fullness in the upper abdomen, upper abdominal pain, belching, nausea, vomiting and heartburn (dyspepsia)
- stomach and intestinal pain
- dark saliva
- bruxism (grinding of teeth)
- hiccups
- stomach and intestinal bleeding
- burning tongue
- duodenal ulcers.

Skin and subcutaneous tissue disorders:

Uncommon:

- fluid accumulation (oedema)

Rare:

- sudden build-up of fluid in the skin and mucous membranes (e.g. throat and tongue), breathing difficulties and/or itching and skin rash, often appearing as an allergic reaction (angioedema)
- skin rash with severe itching and the formation of wheals (urticaria)
- itching
- facial redness
- hair loss
- skin rash
- increased sweating
- dark sweat
- in children, allergy-related bleeding in the skin and gastrointestinal tract wall (Schönlein-Henoch purpura).

Musculoskeletal and connective tissue disorders

Uncommon:

- muscle spasms.

Renal and urinary disorders:

Uncommon:

- dark urine

Rare:

- urine retention
- involuntary passing of urine
- persistent erection (priapism).

General disorders and administration site conditions

Uncommon:

- weakness
- feeling of being unwell (malaise)
- hot flushes
- asthenia

You may experience the following side effects:

- inability to resist the impulse to perform an action that could be harmful, which may include:
 - Strong impulse to gamble excessively despite serious personal or family consequences.
 - Altered or increased sexual interest and behaviour of significant concern to you or to others, for example, an increased sexual drive.
 - uncontrollable excessive shopping or spending
 - binge eating (eating large amounts of food in a short time period) or compulsive eating (eating more food than normal and more than is needed to satisfy your hunger)

Tell your doctor if you experience any of these behaviors; they will discuss ways of managing or reducing the symptoms.

Reporting of side effects

If you get any side effects, talk to your doctor or pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; E-mail: medsafety@hpra.ie. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Apodespan PR

-Children: Keep out of the reach and sight of children

-Use by Date: Do not take Apodespan PR 50 mg/200 mg after the expiry date which is stated on the blister, HDPE label and carton after 'EXP.' The expiry date refers to the last day of that month.

HDPE bottle pack should be used within 2 months after first opening.

- Storage conditions:

This medicinal product does not require any special storage conditions.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. Contents of the pack and other information

What Apodespan PR contains

Apodespan PR contains two active substances i.e.

Each prolonged release tablet contains 50 mg of Carbidopa and 200 mg of Levodopa

The other ingredients are:

Cellulose microcrystalline, Lactose monohydrate, Ferric oxide red (E172), Ferric oxide yellow (E172), Hypromellose K4M, Hypromellose E5, Silica, colloidal anhydrous, Magnesium stearate

What Apodespan PR looks like and contents of the pack

Apodespan PR 50 mg/200 mg Prolonged-Release Tablets:

Peach to light peach colored with mosaic appearance, oval shaped, biconvex tablets of approximately 13.0 mm in length and approximately 7.0 mm in width debossed with 'L200' on one side and plain on other side.

Apodespan PR are available in the following pack sizes:

Blister(s) in outer carton:

Alu/Alu blister of 10, 20, 30, 49, 50, 56, 60, 84, 98, 100, 196, 200 and/or 300 Tablets.

HDPE bottle inserted with cotton and desiccant, fitted with PPCRC closure. Each bottle contains 30, 56, 84 and/or 100 tablets.

Not all pack sizes may be marketed.

Marketing authorisation holder and manufacturer

Accord Healthcare Limited,
Sage house, 319 Pinner road,
Harrow, HA1 4HF
United Kingdom

Name of the member state	Name of the medicinal product
Czech Republic	Carbidopa /Levodopa Accord 50/200 mg tablety s prodlouženým uvolňováním
Germany	Levodopa/Carbidopa Accord 200/50 mg Retardtabletten Levodopa/Carbidopa Accord
Spain	Levodopa/Carbidopa Accord 200/50 mg comprimidos de liberación prolongada
Finland	Levodopa/Carbidopa Accord 200/50 mg depottabletit

Ireland	Apodespan PR 50 mg/200 mg Prolonged release tablets
Italy	CARBIDOPA E LEVODOPA ACCORD
Lithuania	Carbidopa/Levodopa Accord 50/200 mg pailginto atpalaidavimo tabletės
The Netherlands	Levodopa/carbidopa Accord 200/50 mg, tabletten met verlengde afgifte
Poland	Carbidopa + Levodopa Accord
Sweden	Levodopa/Carbidopa Accord
United Kingdom	Apodespan PR 50/200 mg Prolonged release tablets

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