

INFORMATION FOR THE USER

COMBIPAR

Levodopa / Carbidopa / Entacapone

50/12.5/200 mg - 100/25/ 200 mg - 150/37.5/200 mg - 200/50/200 mg

Film-Coated Tablet

For oral use

Active substance:

- Each film tablet contains 50 mg levodopa, 12.5 mg carbidopa and 200 mg entacapone.
- Each film tablet contains 100 mg levodopa, 25 mg carbidopa and 200 mg entacapone.
- Each film tablet contains 150 mg levodopa, 37.5 mg carbidopa and 200 mg entacapone.
- Each film tablet contains 200 mg levodopa, 50 mg carbidopa and 200 mg entacapone.

Excipients in the tablet core: Croscarmellose Sodium, Microcrystalline Cellulose, Poloxamer 188, Hydroxy Propyl Cellulose (LFP), Lactose Monohydrate, Isopropyl Alcohol, Magnesium Stearate

Excipients in the film-coating of 50/12.5/200 mg, 100/25/200 mg and 150/37.5/200 mg:

Opadry Pink 13M240003*, Pure Water, Hydroxy Propyl Cellulose (Klucel LF), Isopropyl Alcohol

Excipients in the film-coating of 200/50/200 mg:

Opadry Red 13M250002**, Pure Water, Hydroxy Propyl Cellulose (Klucel LF), Isopropyl Alcohol

*Opadry Pink 13M240003 Content: Hypromellose 2910, Titanium Dioxide, Glycerin, Red Iron Oxide, Yellow Iron Oxide, Magnesium Stearate, Polysorbate 80

**Opadry Red 13M250002 Content: Hypromellose 2910, Titanium Dioxide, Glycerin, Red Iron Oxide, Magnesium Stearate, Polysorbate 80

Because it contains important information for you, read all of this LEAFLET carefully before you start taking this medicine.

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor or your pharmacist.
- This medicine has been prescribed for you personally. Do not pass it on to others.
- Tell your doctor you are taking this medicine if you go to a doctor or to a hospital.
- Follow the instructions in this leaflet. Do not use higher or lower dose than the dose that is recommended for you.

In this leaflet there are the titles of:

1. What COMBIPAR is and what it is used for
2. Before you take COMBIPAR
3. How to take COMBIPAR
4. Possible side effects
5. How to store COMBIPAR

1. What COMBIPAR is and what it is used for

COMBIPAR contains three active substances in one film-coated tablet. Each film-coated tablet contains levodopa, which is used for the treatment of Parkinson’s disease, and carbidopa and entacapone that increase therapeutic effects of levodopa in Parkinson’s disease. COMBIPAR is a member of drug class named as anti-parkinsonian dopaminergic drug. Your doctor gives you COMBIPAR to treat your Parkinson’s disease. Parkinson’s disease is a disorder of the nervous system. It is caused by a lack of dopamine, a natural substance that is produced in the brain. Dopamine relays messages in the part of the brain that controls muscle movement. When too little dopamine is produced, problems with movement result. Levodopa works by increasing the level of dopamine in the brain. COMBIPAR aids to relieve the symptoms of Parkinson’s disease, such as shaking of the limbs, and stiffness and slowness of movement, which make it difficult to perform normal daily activities.

You may also be given other medicines to help treat this condition.

If you have any questions about how this medicine works or why this medicine has been prescribed for you, ask your doctor.

2. Before you take COMBIPAR

DO NOT TAKE COMBIPAR if you

- are allergic to levodopa, carbidopa or entacapone, or any of the other ingredients of COMBIPAR
- have a severe liver disease
- have narrow-angle glaucoma (an eye disorder in which the pressure in the eye increases)
- have a tumor of the adrenal gland (known as pheochromocytoma; this may increase the risk of severe high blood pressure)
- are taking certain medicines for treating depression (selective MAO-A and MAO-B inhibitors, or non-selective MAO-inhibitors)
- have ever had neuroleptic malignant syndrome (NMS – this is a rare reaction to medicines used to treat severe mental disorders)
- have ever had a disorder with a damage in muscle cells (rhabdomyolysis, a rare muscle disorder)

TAKE SPECIAL CARE with COMBIPAR if you

- have ever had a heart attack, shortness of breath (asthma) or any other diseases of the heart, the blood vessels or the lungs,
- have liver failure,
- have severe kidney failure,
- have ever had a disorder of the kidneys, the liver, or related to hormones,
- have ever had inflammatory intestinal disorder,
- have ever had gastric ulcer,
- have ever had convulsion,
- have ever had any form of severe mental disorder,
- feel depressed, have suicidal thoughts, or notice unusual changes in your mood or behavior,
- have chronic wide-angle glaucoma, because your dose may need to be adjusted and the pressure in your eyes may need to be monitored,
- are taking a medicine which may cause low blood pressure. You should be aware of that COMBIPAR may increase this effect.
- notice that uncontrolled movements begin or get worse after you started to take COMBIPAR. If this happens, your doctor may need to change the dose of your antiparkinson medicine,
- if your doctor told you that you cannot tolerate some sugars. In this case consult your doctor before taking this medicine.
- 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 behaviors are called impulse control disorders and can include addictive gambling, excessive eating or spending, an abnormally high sex drive or a preoccupation with an increase in sexual thoughts or feelings. Your doctor may need to review your treatments.
- find yourself suddenly falling asleep, or if you feel very drowsy (see also section 'Driving and using machines'),
- notice that your muscles get very rigid or jerk violently, or if you get tremors, agitation, confusion, fever, rapid pulse, or wide fluctuations in your blood pressure,
- have diarrhea. In this case your doctor may want to monitor your weight to prevent excessive weight loss.
- experience progressive anorexia, asthenia (weakness, exhaustion) and weight decrease within a relatively short period of time. If this happens, your doctor may want to perform a general medical evaluation including liver function,
- will have surgery taking general anesthesia. In this case tell your doctor you are taking COMBIPAR,
- feel the need to stop using COMBIPAR,contact your doctor firstly. In order to prevent side effects and worsening of your Parkinson symptoms it may be necessary to decrease COMBIPAR dose gradually and to make changes in your other anti-parkinson medicines.

If these warnings are valid for you even if in the past, please consult your doctor.

Taking COMBIPAR with food and drink

You can take COMBIPAR with or without food.

For some patients, COMBIPAR may not be well absorbed if it is taken with, or shortly after eating protein-rich food (such as meats, fish, dairy products, seeds and nuts). Consult your doctor if you think this applies to you.

Do not take COMBIPAR and medicines containing iron concomitantly at the same time by oral route. After taking one of them, wait at least 2 to 3 hours before taking the other.

Pregnancy

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

If you are pregnant or think you may be pregnant, do not take COMBIPAR without consulting your doctor. COMBIPAR must not be used in pregnancy unless clearly necessary.Your doctor will explain potential risks of COMBIPAR use in pregnancy.

If you noticed you became pregnant during your treatment, immediately consult your doctor or pharmacist.

Breast-feeding

Consult your doctor or pharmacist before taking this drug.

If you are breast-feeding tell your doctor. You must not breast-feed your baby when you are taking COMBIPAR therapy.

Driving and using machines

COMBIPAR may lower your blood pressure, which may make you feel light-headed or dizzy. Therefore, be particularly careful when you drive or when you use any tools or machines.

If you feel very drowsy, or if you sometimes find yourself suddenly falling asleep, you must not drive or do anything else that requires you to be alert (you must not drive or use machines). Take your doctor’s advice for this condition. Otherwise, you may put yourself and others at risk of serious injury or death.

Important information about some excipients in COMBIPAR

COMBIPAR tablets contain lactose. If your doctor told you that you have a problem in digestion of some sugars contact your doctor before taking this medicine.

This medicinal product contains sodium less than 1 mmol (23 mg) in each dose, therefore, "it does not contain sodium."

This medicinal product contains glycerin less than 10 g; therefore, no warning is necessary for glycerin content.

Using other medicines

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines, including medicines that are given to decrease your blood pressure, and medicines obtained without a prescription and herbal medicines.

COMBIPAR may increase the effects and side effects of some antidepressants and certain medicines. These include:

- Medicines that inhibit MAO-A enzyme (e.g., moclobemide),
- Tricyclic antidepressants (e.g., amitriptyline)
- Noradrenaline reuptake inhibitors (e.g., desipramine, maprotiline, and venlafaxine),
- Paroxetine, rimiterole, isoprenaline, adrenalin, noradrenalin, dopamine, dobutamine, alpha-methylidopa and apomorphine.

If you take these medicines while you are taking COMBIPAR therapy, you should be aware of increased effects.

The effects of COMBIPAR may be weakened by certain medicines. These include:

- medicines used to treat mental disorders (dopamine antagonists)
- medicines used to treat nausea and vomiting (dopamine antagonists)
- medicines used to prevent convulsions (phenytoin)
- medicines used to relax the muscles (papaverine).

If you are taking these medicines or if you notice that COMBIPAR does not act as before when you are taking these medicines tell your doctor.

COMBIPAR may make it harder for you to digest iron. Therefore, do not take COMBIPAR and iron supplements at the same time. After taking one of them, wait at least 2 to 3 hours before taking the other.

Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines with or without prescription.

3. How to take COMBIPAR

• Directions on proper usage and dose/administration frequency:

Always take COMBIPAR exactly as your doctor has told you. You should check with your doctor or pharmacist if you are not sure.

Your doctor will tell you exactly how many tablets of COMBIPAR to take each day. Depending on how you respond to the treatment, your doctor may suggest a higher or a lower dose.

For COMBIPAR 50/12.5/200 mg, COMBIPAR 100/25/200 mg or COMBIPAR 150/37.5/200 mg film-coated tablets, do not take more than 10 tablets per day. For COMBIPAR 200/50/200 mg film-coated tablets, do not take more than 7 tablets per day.

Strictly follow your doctor’s instructions on how and when to use your COMBIPAR, other levodopa medicines and other Parkinson medicines. If there are conditions in the instructions or in the leaflet that you are not sure, consult your doctor or your pharmacist.

Administration route and method:

Take the tablet with some water (e.g., 1 glass of water). Each COMBIPAR tablet contains one full doses of levodopa, carbidopa and entacapone. Always take only one tablet at each dose. Do not break the tablets into halves.

Some age groups:

Use in children:

Because COMBIPAR use is not approved in children and adolescents under 18 years of age, its use in this population is not recommended.

Use in elderly:

If you are over 65 years of age, you can use COMBIPAR without dose adjustment.

Special uses:

Kidney/Liver failure:

COMBIPAR treatment should be applied to patients with severe kidney failure including those who are receiving dialysis.

It is recommended to be cautious when COMBIPAR is administered to patients with mild to moderate liver failure. A dose reduction may be necessary. Unless otherwise is recommended by your doctor, follow these instructions.

Your doctor will tell you how long you should take COMBIPAR treatment. Do not stop the treatment early; this may cause worsening of your disease.

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

If you take more COMBIPAR than you should:

Contact your doctor or pharmacist if you took more COMBIPAR than you should.

If you forget to take COMBIPAR:

If it is more than 1 hour until your next dose: Take one tablet as soon as you remember, and the next tablet at the normal time.

If it is less than 1 hour until your next dose: Take a tablet as soon as you remember, wait 1 hour, then take another tablet. After that, carry on as normal. Always leave at least an hour between COMBIPAR tablets, to avoid possible side effects.

If you are not sure, consult your doctor.

Do not take a double dose to make up for a forgotten tablet.

If you stop taking COMBIPAR

Do not stop taking COMBIPAR unless your doctor tells you to. In such a case your doctor may need to adjust your other antiparkinson medicines, especially levodopa, to give sufficient control of your symptoms. If you suddenly stop taking COMBIPAR and other antiparkinsonian medicines it may result in unwanted side effects (e.g., severe muscle stiffness, high fever, changes in consciousness).

4. Possible side effects

Like all medicines, side effects may be occurred in patients sensitive to substances in COMBIPAR.

If you experience any of the following, stop taking COMBIPAR and IMMEDIATELY contact your doctor or admit to emergency department of nearest hospital to you:

- Allergic reaction signs may include hives (urticaria), itching, rash, swelling of your face, lips, tongue or throat. This may cause difficulties in breathing or swallowing.
- Your muscles get very rigid or jerk violently, you get tremors, agitation, confusion, fever, rapid pulse, or wide fluctuations in your blood pressure. These can be symptoms of neuroleptic malignant syndrome (NMS, a rare severe reaction to medicines used to treat disorders of the central nervous system) or rhabdomyolysis (a rare severe muscle disorder).

All of these are very serious side effects. If you experience any of these side effects,contact your doctor as soon as possible.

You may need urgent medical intervention or hospitalization.

The following side effects may occur due to COMBIPAR use:

The side effects are listed based on the following categories:

Very common	affects more than 1 user in 10
Common	affects 1 to 10 users in 100
Uncommon	affects 1 to 10 users in 1,000
Rare	affects 1 to 10 users in 10,000
Very rare	affects less than 1 user in 10,000
Not known	frequency cannot be estimated from the available data.

Very common

- Uncontrolled movements (dyskinesias)
- Feeling sick (nausea)
- Harmless reddish-brown discoloration of urine
- Muscle pain
- Diarrhea

Common

- Heart or artery disease events (e.g. Chest pain) other than heart attack
- Irregular heart rate or rhythm
- Light-headedness or fainting due to low blood pressure,
- High blood pressure
- Worsening of parkinson's symptoms
- Dizziness
- Drowsiness
- Vomiting
- Abdominal pain and discomfort
- Heartburn
- Dry mouth
- Constipation
- Inability to sleep
- Hallucinations
- Confusion
- Abnormal dreams including nightmares
- Mental changes including problems with memory and thought problems
- Anxiety and depression (possibly with thoughts of suicide)
- Tiredness
- Chest pain
- More frequent falling
- Gait disturbance
- Loss of power and energy
- Shortness of breath
- Increased sweating
- Rashes
- Muscle cramps
- Involuntary muscle contractions
- Swelling of legs
- Blurred vision
- Anemia
- Decreased appetite
- Decreased weight
- Headache
- Joint pain
- Urinary tract infection

Uncommon

- Heart attack
- Bleeding in the gut
- Abnormal liver function tests
- Psychotic symptoms
- Inflammation of the colon
- Discolorations in skin, hair, beard, and nail
- Changes in the blood cell count which may result in bleeding
- Swallowing difficulties
- Inability to urinate
- Feeling bad

Rare

- Convulsions

Unknown

- Yellowing in skin or conjunctiva (jaundice)
- Itching
- Excessive sleepiness in daytime
- Suddenly falling asleep

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 behavior 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.

If you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

5. How to store COMBIPAR

Keep COMBIPAR out of the reach and sight of children, and in its package.

Store at temperature below 25°C.

Use it in conformity with expiry date.

Do not use COMBIPAR after the expiry date which is stated on the package.

If you noticed damage in the product or its package, do not use COMBIPAR.

Marketing Authorization Holder:

Pharmaline – Lebanon
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Contact us: pharmaline@mailagroup.com

Reg. № Lebanon for COMBIPAR 50/12.5/200 mg	101616/1
Reg. № Lebanon for COMBIPAR 100/25/ 200 mg	101716/1
Reg. № Lebanon for COMBIPAR 150/37.5/200 mg	101816/1
Reg. № Lebanon for COMBIPAR 200/50/200 mg	178517/1

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