CO-BENELDOPA 50 mg/12.5 mg, 100 mg/25 mg AND 200 mg/50 mg CAPSULES

levodopa/benserazide

Package leaflet: Information for the patient

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 or pharmacist.
- 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 or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

1 What Co-Beneldopa is and what it is used for

Co-Beneldopa contains two active substances (levodopa and benserazide) in one capsule.

Levodopa, is a precursor of a substance called dopamine which is made by the body. A lack of dopamine in certain parts of the brain is a cause of Parkinson's disease. Levodopa increases the amount of dopamine and hence helps to improve the symptoms of Parkinson's disease. The second active substance benserazide inhibits the breakdown of the active substance levodopa in the body so that a lower levodopa dose can be given.

Co-Beneldopa is used to treat the symptoms of Parkinson's disease (shaking palsy, a disease characterised by coarse tremors, slowed movements and muscular rigidity).

2 What you need to know before you take Co-Beneldopa

Do not take Co-Beneldopa
- if you are allergic to levodopa, benserazide or any of the other ingredients of this medicine (listed in section 6);
- if you have hyperthyroidism (an overactive thyroid gland), or phaeochromocytoma (a tumour of the adrenal gland that causes hypertension);
- if you have an excessively high blood cortisol level (Cushing's syndrome);
- if you have a severe disorder of the metabolism, liver, kidneys or bone marrow;
- if you have severe heart disease, such as a severe heartbeat disorder (tachycardia), severe cardiac arrhythmia or heart failure;
- if you have psychosis (a psychiatric condition characterised by personality derangement and loss of contact with reality);
- if you have narrow angle glaucoma (high pressure in the eye);
- if you are under 25 years of age. This is because your bones may not have finished developing;
- if you are pregnant;
- if you are a woman of child-bearing age not using reliable contraception (see section 'Pregnancy and breast-feeding')
- if you are taking reserpine (used to treat high blood pressure);
- if you are taking a non-selective monoamine oxidase (MAO) inhibitor (e.g. tranylcypromine (used to treat depression)) or a combination of a MAO-A inhibitor (e.g. moclobemid (used to treat depression)) and a MAO-B inhibitor (e.g. selegilin or rasagilin (used to treat Parkinson's disease)). (see 'Other medicines and Co-Beneldopa').

Warnings and precautions
Talk to your doctor or pharmacist before taking this medicine
- if your symptoms were caused by another drug, or if you have another movement disorder called Huntington's chorea, as this medicine may not be appropriate;
- if you have ever had a heart attack or heart problems;
- if you have orthostatic hypotension (low blood pressure associated with changes in posture, which makes you feel light-headed or dizzy);
- if you have ever had a peptic or intestinal ulcer;
- if you have ever had convulsions (fits);
- if you have ever had osteomalacia (a bone disease similar to rickets);
- if you have wide angle glaucoma (high pressure in the eye);
- if you have diabetes. You should check your blood sugar levels more often, and your doctor may need to adjust the dose of your antidiabetic medicine;
- if you are about to undergo surgery.

Depression and suicidal thoughts may occur during treatment with Co-Beneldopa, although they can also be caused by your disease. If you feel depressed whilst on treatment, you should contact your doctor.

Levodopa is associated with somnolence (excessive drowsiness) and, very rarely, with excessive daytime sleepiness and sudden onset sleep episodes. These can occur without warning signs. If you experience these symptoms, you must inform your doctor (see also section 'Driving and using machines').

While taking Co-Beneldopa, you may experience circulatory problems as a result of low blood pressure (see section 4). These symptoms usually disappear or improve when the Co-Beneldopa dose is reduced. If you are elderly, or take medicines to treat high blood pressure or other medicines that may lower your blood pressure, or if you have already experienced circulatory problems as a result of low blood pressure, your doctor should carefully monitor you at the start of treatment in particular or when increasing your dose.

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.

A small subgroup of patients may suffer from cognitive and behavioural disturbances when taking, against medical advice, levodopa/benserazide doses far in excess of those needed for the treatment of motor disorders.

Abrupt withdrawal of Co-Beneldopa after many years of treatment with medicines that contain the same active substances as Co-Beneldopa may result in withdrawal symptoms ('malignant levodopa withdrawal syndrome'). These symptoms may include very high fever, muscle stiffness and psychological abnormalities. Additional signs in severe cases may include excretion of muscle protein in urine (myoglobinuria), breakdown of muscle fibres (rhabdomyolysis), acute kidney failure or complete inability to move. These conditions are life-threatening. If this happens to you, call the nearest available doctor straight away.

Gastrointestinal symptoms, such as dry mouth, nausea, vomiting and diarrhoea, may occur particularly at the start of treatment (see section 4). These symptoms can largely be reduced or avoided by taking Co-Beneldopa with some low protein food or a drink, or by increasing the dose more slowly.

Movements you cannot control may develop after taking this medicine for a prolonged period of time and/or in high doses (see section 4.). These disturbances usually resolve or improve after reducing the dose.

Patients with Parkinson's disease have been observed to have a higher risk of developing black skin cancer compared to the general population. It is unknown whether the increased risk observed is due to Parkinson's disease or other factors such as treatment with levodopa. While taking Co-Beneldopa you should therefore regularly examine your skin for suspicious changes and have regular skin examinations performed by appropriately qualified individuals (e.g. dermatologists).

Your doctor should carry out certain periodic tests, such as taking blood and urine samples and checking your heart rate and blood pressure.

Other medicines and Co-Beneldopa
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

The effect of the following active substances or groups of medicines may be influenced when Co-Beneldopa is taken at the same time as any of these medicines:
- Medicines used to treat low blood pressure, circulatory failure, irregular heart beat; to reduce or stop uterine contractions; and to control spasms of the lower airways ('sympathomimetic agents'): The effect of sympathomimetic agents may be increased. Co-administration is therefore not recommended. If the concomitant application should be indispensable, your doctor may need to adjust the dose of your sympathomimetic treatment.
- Medicines used to treat high blood pressure ('antihypertensive agents'): The effect of antihypertensive agents may be increased, thus increasing the risk of drops in blood pressure. Blood pressure must therefore be monitored regularly (see above). If necessary, your doctor will adjust the dose of Co-Beneldopa and/or the dose of the antihypertensive agent.

The effect of Co-Beneldopa may be influenced by other medicines as follows:
- Its effect may be decreased by:
  - certain pain relievers (opioids);
  - medicines used to treat high blood pressure that contain the active substance reserpine. If you are taking such medicines, you must not take Co-Beneldopa (see section 'Do not take Co-Beneldopa');
  - certain medicines with tranquillising effects used to treat mental illnesses (neuroleptic agents).
- Its effect and possibly also its side effects may be increased by:
  - medicines that contain the active substance selegiline (for the treatment of Parkinson's disease).
- Other possible interactions:
  - Certain medicines used to treat depression ('MAO inhibitors'): Co-administration of Co-Beneldopa with medicines that contain the active substance tranylcypromine may produce dangerously high blood pressure. This might also happen as late as 2 weeks after stopping tranylcypromine. If you are taking such medicines, you must not take Co-Beneldopa (see section 'Do not take Co-Beneldopa'). There must therefore be an interval of at least 2 weeks between discontinuation of tranylcypromine and the start of treatment with Co-Beneldopa. Co-administration of Co-Beneldopa with moclobemide or selegiline or rasagiline is, however, considered to be safe.
  - In Parkinson's patients, it has been observed that co-administration of Co-Beneldopa with domperidone may cause increased levels of the active substance levodopa in the blood. Co-administration may increase the risk of heart rhythm disorders.

It is possible to take Co-Beneldopa together with other medicines for Parkinson's disease (e.g. dopamine agonists, amantadine, anticholinergic agents, selegiline, bromocriptine), but both the desired and the undesired effects of treatment may be intensified, and it may be necessary for your doctor to prescribe a lower dose of Co-Beneldopa or of the other medicine for you. When starting add-on treatment with a medicine that contains the active substance entacapone, it may also become necessary to reduce the dose of Co-Beneldopa.

Operations
If you are going to have an operation, tell the doctor that you are taking Co-Beneldopa. This is because you may need to stop taking it before you have a general anaesthetic.

Co-Beneldopa with food and drink
Taking Co-Beneldopa with high-protein meals should be avoided because these could reduce the effect of Co-Beneldopa.
When possible, you should take Co-Beneldopa at least 30 minutes before or 1 hour after meals.

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

It is recommended that you take a pregnancy test to exclude that you are pregnant before initiating the treatment with Co-Beneldopa. You must not take Co-Beneldopa if you are pregnant. If you are of child-bearing age, you must use reliable contraception during treatment with Co-Beneldopa. Nevertheless, if you still become pregnant or think you may be pregnant, you must consult your doctor. He/she will advise you how to stop treatment with Co-Beneldopa.

You should not breast-feed during treatment with Co-Beneldopa. If treatment with Co-Beneldopa is necessary during lactation, you should stop breast-feeding your baby.

Driving and using machines
Levodopa/benserazide may significantly affect your ability to drive and use machines.
Levodopa is associated with somnolence (excessive drowsiness) and, very rarely, with excessive daytime sleepiness and sudden onset sleep episodes. These can occur without warning signs. If you experience these symptoms, you must inform your doctor and you must refrain from driving or engaging in activities where impaired alertness may put yourself or others at risk of serious injury (e.g. operating machines), until such recurrent episodes and somnolence have been resolved.

3 How to take Co-Beneldopa

Always take this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.
[50 mg/12.5 mg strength:]
Treatment with Co-Beneldopa is usually started with low doses, e.g. one capsule two to four times a day.
[100 mg/25 mg strength:]
Treatment with Co-Beneldopa is usually started with low doses. Co-Beneldopa 100 mg/25 mg Capsules are not appropriate for this and the 50 mg/12.5 mg strength is available for this purpose.
[200 mg/50 mg strength:]
Treatment with Co-Beneldopa is usually started with low doses. Co-Beneldopa 200 mg/50 mg Capsules are not appropriate for this and the 50 mg/12.5 mg strength is available for this purpose.
[50 mg/12.5 mg strength:]
After three to seven days, your doctor may, if necessary, begin to increase your dose by one or two capsules every third to seventh day, until you achieve suitable control of your symptoms.
[100 mg/25 mg strength:]
After three to seven days, your doctor may, if necessary, begin to increase your dose by one capsule every third to seventh day, until you achieve suitable control of your symptoms.
[200 mg/50 mg strength:]
After three to seven days, your doctor may, if necessary, begin to increase your dose every third to seventh day, until you achieve suitable control of your symptoms. Co-Beneldopa 200 mg/50 mg Capsules are not appropriate for this and other strengths are available to this end.
The maximum dose is generally no more than
[50 mg/12.5 mg:]
sixteen capsules a day.
[100 mg/25 mg:]
eight capsules a day.
[200 mg/50 mg:]
four capsules a day.
The daily dose should be spread out over the day into several smaller doses. The size of individual doses and the way they are spread throughout the day must be adjusted to suit the needs of each individual patient.
It may take several weeks for the full effect of your medicine to become apparent.
If you have previously taken levodopa on its own or with another decarboxylase inhibitor, you should stop taking it twelve hours before you start taking Co-Beneldopa.
When possible, you should take Co-Beneldopa at least 30 minutes before or 1 hour after meals. You must swallow the capsules whole, without chewing them, with a drink.

If you take more Co-Beneldopa than you should
If you (or someone else) swallow a lot of the capsules all together, or if you think a child has swallowed any of the capsules, contact your nearest hospital casualty department or your doctor immediately. Please take this leaflet, any remaining capsules and the container with you to the hospital or doctor so that they know which capsules were consumed.
Overdose may cause a worsening of your symptoms, as well as confusion, hallucinations and sleep disturbances. Nausea and vomiting (feeling and being sick) and abnormal heart rhythms may rarely occur.

If you forget to take Co-Beneldopa
Do not take a double dose to make up for a forgotten dose. Take your next dose as usual; however, you may experience some return of Parkinson's disability in the meantime.

If you stop taking Co-Beneldopa
Your doctor will advise you when you should stop taking Co-Beneldopa. Usually, it is taken for a long time since it replaces a substance, dopamine, which is not produced in sufficient amounts by patients with Parkinson's disease.
You must tell your doctor if you want to stop taking Co-Beneldopa. Although it is rare, sudden discontinuation of treatment can cause potentially life-threatening side effects, including a condition called neuroleptic malignant-like syndrome, which involves greatly elevated body temperature, muscle stiffness and psychological changes, and akinetic crisis (inability to move). To avoid these, your doctor will advise you how to end your treatment.
If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4 Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

If you get the following side effects, contact your doctor immediately:
- allergic reactions. The signs include a rash and feeling itchy.
- heart beat that is uneven or faster or slower than normal.
- low numbers of all types of white blood cells (leukopenia). The signs include infections of your mouth, gums, throat and lungs.

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.

Other possible side effects:

Not known (frequency cannot be estimated from the available data)
- febrile infections, bronchitis, common cold
- low number of red blood cells (anaemia). The signs include feeling tired, pale skin, palpitations (a fluttering sensation in your heart) and being short of breath
- low number of platelets in your blood (thrombocytopenia). The signs include bruising easily and nose bleeds
- decreased appetite
- Cognitive and behavioural disturbances after taking levodopa/benserazide in doses far in excess of the required dose (see section 2)
- confusion, depression
- agitation, especially in the elderly
- anxiety, especially in the elderly
- having difficulty sleeping (insomnia), especially in the elderly
- hallucinations, especially in the elderly
- delusions, especially in the elderly
- disorientation, especially in the elderly
- taste loss, taste alterations
- uncontrolled movements (dyskinesia)*
- fluctuations in response such as 'freezing' (movement suddenly becoming difficult), 'end-of-dose' (a return of symptoms before the next dose of medicine is due) and 'on-off' phenomena (sudden changes from periods of good symptom control to periods where symptoms are less controlled)*
- somnolence, excessive daytime sleepiness, falling asleep suddenly
- dizziness, headache
- dry mouth
- drop in blood pressure as a result of standing up from a sitting or lying position (sometimes accompanied by dizziness). This usually gets better if your dose is lowered
- nausea, vomiting, diarrhoea
- discoloured saliva, tongue, tooth or mouth
- increased levels of some liver enzymes, such as liver transaminases, alkaline phosphatase or gamma-glutamyltransferase
- discoloured urine, usually red-tinged
- increased levels of the substances uric acid or urea nitrogen in blood.

* In the later stages of treatment, and in many cases after the medicine has been taken for many years, uncontrollable, unusual movements of the arms, legs, face and tongue or fluctuations in response can occur. These may disappear if the daily dose is changed or if the spread of doses throughout the day can be improved.

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 Co-Beneldopa

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 bottle and outer packaging after EXP. The expiry date refers to the last day of that month.
This medicinal product does not require any special storage conditions.
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 to protect the environment.

6 Contents of the pack and other information

What Co-Beneldopa contains
- The active substances are levodopa and benserazide.
- Each capsule contains 50 mg levodopa and 12.5 mg benserazide (as hydrochloride).
- Each capsule contains 100 mg levodopa and 25 mg benserazide (as hydrochloride).
- Each capsule contains /200 mg levodopa and 50 mg benserazide (as hydrochloride).
- The other ingredients are as follows:
  Capsule contents: mannitol, cellulose microcrystalline, povidone K-30, talc, magnesium stearate
  Capsule shell: gelatin, titanium dioxide (E171), black iron oxide (E172), [200/50 mg:] red iron oxide (E172), erythrosin (E127), indigo carmine (E132).
  Printing ink: shellac, propylene glycol, potassium hydroxide, black iron oxide.

What Co-Beneldopa looks like and contents of the pack
- Co-Beneldopa 50 mg/12.5 mg Capsules are hard gelatin capsules with an opaque grey cap imprinted '62.5' axially in black ink, and an opaque blue body imprinted 'BL' axially in black ink, and filled with off-white to brownish white granules.
- Co-Beneldopa 50 mg/12.5 mg Capsules are available in white opaque bottles with a white cap with desiccant containing 20, 30, 50, 60, 90 and 100 capsules.
- Co-Beneldopa 100 mg/25 mg Capsules are hard gelatin capsules with an opaque pink cap imprinted '125' axially in black ink, and an opaque blue body imprinted 'BL' axially in black ink, and filled with off-white to brownish white granules.
- Co-Beneldopa 100 mg/25 mg Capsules are available in white opaque bottles with white cap with desiccant containing 20, 30, 50, 60, 90 and 100 capsules in container.
- Co-Beneldopa 200 mg/50 mg Capsules are hard gelatin capsules with an opaque maroon cap imprinted '250' axially in black ink, and an opaque blue body imprinted 'BL' axially in black ink, and filled with off-white to brownish white granules.
- Co-Beneldopa 200 mg/50 mg Capsules are available in white opaque bottles with white cap with desiccant containing 20, 30, 50, 60 and 100 capsules in container.

  Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer
Marketing authorisation holder: Teva UK Limited, Ridings Point, Whistler Drive, Castleford, WF10 5HX, United Kingdom
Company responsible for manufacture: TEVA Pharmaceutical Works Private Limited Company, Pallagi út 13, 4042 Debrecen, Hungary.

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