Patient leaflet in accordance with the Pharmacists' Regulations (Preparations) - 1986

This medicine is dispensed with a doctor's prescription only

Entresto 50 mg **Film-coated tablets**	**Entresto 100 mg** **Film-coated tablets**	**Entresto 200 mg** **Film-coated tablets**
Active ingredient: Each film-coated tablet contains: 24 mg sacubitril and 26 mg valsartan as sodium salt complex	**Active ingredient:** Each film-coated tablet contains: 49 mg sacubitril and 51 mg valsartan as sodium salt complex	**Active ingredient:** Each film-coated tablet contains: 97 mg sacubitril and 103 mg valsartan as sodium salt complex

Inactive ingredients and allergens in the medicine - see section 2 'Important information about some of this medicine's ingredients' and section 6 'Additional information'.

Read the entire leaflet carefully before you start using this medicine. This leaflet contains concise information about this medicine. If you have any further questions, consult your doctor or pharmacist.
This medicine has been prescribed to treat your illness. Do not pass it on to others. It may harm them, even if it seems to you that their illness is similar to yours.

1. What is this medicine intended for?

Entresto is indicated for the treatment of heart failure (NYHA class II-IV) in patients with systolic dysfunction.

Entresto has been shown to reduce the rate of cardiovascular death and heart failure hospitalisation compared to angiotensin converting enzyme (ACE) inhibitor therapy.

Therapeutic group:
Entresto belongs to a group of medicines that act on the renin-angiotensin system; angiotensin II receptor blockers (ARBs), different combinations.

Heart failure occurs when the heart is weak and cannot pump enough blood to the lungs and the rest of the body. The most common symptoms of heart failure are breathlessness, fatigue, tiredness and ankle swelling.

2. Before using this medicine

Do not use this medicine if:

- you are sensitive (allergic) to the active ingredients sacubitril, valsartan or to any of the other ingredients in this medicine (listed in section 6).
- you are taking another type of medicine called an angiotensin converting enzyme (ACE) inhibitor (for example enalapril, lisinopril or ramipril), which is used to treat high blood pressure or heart failure. If you have been taking an angiotensin converting enzyme (ACE) inhibitor, wait for 36 hours after taking the last dose before you start to take Entresto (see 'Drug interactions').
- you have ever had a reaction called angioedema (rapid spreading of swelling under the skin in areas such as the face, throat, arms and legs which can be life threatening if throat swelling blocks the airway) when taking an ACE inhibitor or an angiotensin receptor blocker (ARB) (such as valsartan, telmisartan or irbesartan).
- you have a history of angioedema which is hereditary or for which the cause is unknown (idiopathic).

- you have diabetes or impaired kidney function and you are being treated with a blood pressure lowering medicine containing aliskiren (see 'Drug interactions').
- you have a severe liver disease.
- you are more than 3 months pregnant (see 'Pregnancy and breast-feeding').

If any of the above applies to you, do not take Entresto and inform your doctor.

Special warnings about using this medicine
Talk to your doctor before or when taking Entresto if:

- you are being treated with an angiotensin receptor blocker (ARB) or aliskiren (see 'Do not use this medicine if').
- you have ever had angioedema (see 'Do not use this medicine if' and section 4 'Side effects').
- you experience abdominal pain, nausea, vomiting or diarrhoea after taking Entresto. Your doctor will decide on further treatment. Do not stop taking Entresto on your own.
- you have low blood pressure or are taking other medicines that reduce your blood pressure (for example, medicines that increase urine production (diuretics)) or are suffering from vomiting or diarrhoea, especially if you are aged 65 years or more, or if you have kidney disease and low blood pressure.
- you have kidney disease.
- you are suffering from dehydration.
- your kidney artery has narrowed.
- you have liver disease.
- you have hallucinations, paranoia or changes in sleeping pattern while taking Entresto.
- your systolic blood pressure is lower than 100 mmHg.
- you have hyperkalaemia (high levels of potassium in the blood).
- if you suffer from heart failure classified as NYHA class IV (unable to carry on any physical activity without discomfort and may have symptoms even when resting).

If any of the above conditions applies to you, tell your doctor or pharmacist before taking Entresto.

Children and adolescents
The medicine is not indicated for children and adolescents below the age of 18 years.

Tests and follow-up
Your doctor may check the amount of potassium and sodium in your blood at regular intervals during Entresto treatment. In addition, your doctor may check your blood pressure at the start of treatment and when the dose is increased.

Drug interactions
If you are taking or have recently taken other medicines, including nonprescription medications and dietary supplements, tell your doctor or pharmacist. It may be necessary to change the dose, to take other precautions, or even to stop taking one of the medicines. This is particularly important for the following medicines:

- angiotensin converting enzyme (ACE) inhibitors. Do not take Entresto with ACE inhibitors. If you have been taking an ACE inhibitor, wait 36 hours after taking the last dose of the ACE inhibitor before starting treatment with Entresto (see 'Do not use this medicine if'). If you stop taking Entresto, wait 36 hours after taking your last dose of Entresto before starting an ACE inhibitor.
- other medicines used to treat heart failure or lower blood pressure, such as angiotensin receptor blockers or aliskiren (see 'Do not use this medicine if').
- some medicines in the statin group that are used to lower high cholesterol levels (for example atorvastatin).
- sildenafil, tadalafil, vardenafil or avanafil, which are medicines used to treat erectile dysfunction or lung hypertension.

- medicines that increase the amount of potassium in the blood, including potassium supplements, salt substitutes containing potassium, potassium sparing medicines and heparin.
- painkillers of the type called non-steroidal anti-inflammatory drugs (NSAIDs) or selective cyclooxygenase-2 (Cox-2) inhibitors. If you are taking one of these, your doctor may want to check your kidney function when starting or adjusting treatment (see 'Special warnings about using this medicine').
- lithium, a medicine used to treat some types of psychiatric illness.
- furosemide, a medicine belonging to the type known as diuretics, which are intended to increase the amount of urine you produce.
- nitroglycerine, a medicine used to treat angina pectoris.
- some types of antibiotics (in the rifamycin group), ciclosporin (used to prevent rejection of transplanted organs) or antivirals such as ritonavir (used to treat HIV/AIDS).
- metformin, a medicine used to treat diabetes.

If any of the above conditions applies to you, tell your doctor or pharmacist before taking Entresto.

Using this medicine and food
Entresto can be taken with or without food.

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 for advice before taking this medicine.

Pregnancy –
You should tell your treating doctor if you are (or are planning to become) pregnant.
Your doctor will generally advise you to stop taking this medicine before you become pregnant or as soon as you know you are pregnant and will advise you to take another medicine instead of Entresto.
This medicine is not recommended in early pregnancy and should not be taken when more than 3 months pregnant, as it may cause serious harm to your baby if it is used after the third month of pregnancy.

Breast-feeding –
Entresto is not recommended for mothers who are breast-feeding. Tell your doctor if you are breast-feeding or about to start breast-feeding.

Driving and using machines
Before you drive a vehicle, use tools or operate machines, or carry out other activities that require concentration, make sure you know how Entresto affects you. If you feel dizzy or very tired while taking this medicine, do not drive, cycle or use tools or operate machines.

Important information about some of this medicine's ingredients
This medicine contains less than 1 mmol sodium (23 mg) per 200 mg dose, that is to say essentially 'sodium free'.

3. How should you use the medicine?

Always use this medicine according to your doctor's instructions. Check with your doctor or pharmacist if you are not sure about your dose or about how to take this medicine.
Only your doctor will determine your dose and how you should take this medicine.
The recommended starting dose is usually one tablet of 50 mg or 100 mg twice a day (one tablet in the morning and one tablet in the evening). Your doctor will decide your exact starting dose based on which medicines you were taking previously and your blood pressure. Your doctor will then adjust the dose every 2-4 weeks depending on how you respond to the treatment until the

best dose for you is found. The usual recommended target dose is 200 mg twice a day (one tablet in the morning and one tablet in the evening).

Inform your doctor if you have hyperkalaemia (high blood potassium levels [higher than 5.4 mmol/l]) or your blood pressure is lower than 100 mmHg, as treatment should not be initiated in such conditions.
If your blood pressure is higher than 100 mmHg, but lower than 110 mmHg, your doctor will consider a starting dose of 50 mg twice a day.

Elderly patients -
If you are 75 years old or older, your doctor will consider a starting dose of 50 mg Entresto twice a day.

Patients taking Entresto can develop low blood pressure (dizziness, light-headedness), a high level of potassium in the blood (detected when your doctor performs a blood test) or decreased kidney function. If this happens, your doctor may reduce the dose of any other medicine you are taking, temporarily reduce the Entresto dose, or stop Entresto treatment completely.

Do not exceed the recommended dose.

Swallow the medicine with a glass of water. Entresto can be taken with or without food.
Breaking or crushing the film-coated tablet is not recommended.

If you have accidentally taken a higher dose
If you have taken an overdose, or if a child has accidentally swallowed some medicine, immediately see a doctor or go to a hospital emergency room and bring the medicine package with you. If you experience severe dizziness and/or fainting, contact your doctor as quickly as possible and lie down.

If you forget to take the medicine
It is advisable to take your medicine at the same time each day. However, if you forget to take this medicine at the scheduled time, do not take a double dose to make up for the forgotten one. Take the next dose at the regular time and consult your doctor.
Adhere to the treatment as recommended by your doctor.
Even if your health improves, do not stop taking this medicine without consulting your doctor or pharmacist.
If you stop taking this medicine, your condition may get worse. Do not stop taking your medicine unless your doctor tells you to.

Do not take medicines in the dark! Check the label and dose <u>every time</u> you take medicine. Wear glasses if you need them.
If you have any further questions about using this medicine, consult your doctor or pharmacist.

4. Side effects

Like with all medicines, using Entresto may cause side effects in some users. Do not be alarmed by this list of side effects. You may not experience any of them.

Some side effects can be serious.
Stop taking Entresto and seek immediate medical attention if you notice swelling of the face, lips, tongue and/or throat, which may cause difficulties in breathing or swallowing. These symptoms may be signs of angioedema (an uncommon side effect which may affect up to 1 in 100 users).

Additional side effects
If any of the side effects listed below becomes severe, tell your doctor or pharmacist.

Very common side effects (effects that occur in more than 1 in 10 users):
- low blood pressure, which can cause symptoms of dizziness and light-headedness (hypotension)
- high levels of potassium in the blood, shown in a blood test (hyperkalaemia)
- decreased kidney function (renal impairment)

Common side effects (effects that occur in 1-10 in 100 users):
- cough
- dizziness
- diarrhoea
- low levels of red blood cells, shown in a blood test (anaemia)
- tiredness (fatigue)
- (acute) inability of the kidney to work properly (renal failure)
- low levels of potassium in the blood, shown in a blood test (hypokalaemia)
- headache
- fainting (syncope)
- weakness (asthenia)
- nausea
- low blood pressure (dizziness, light-headedness) when switching from sitting or lying to standing position
- gastritis (stomach pain, nausea)
- spinning sensation (vertigo)
- low levels of sugar in the blood, shown in a blood test (hypoglycaemia)

Uncommon side effects (effects that occur in 1-10 in 1,000 users):
- allergic reaction with rash and itching (hypersensitivity)
- dizziness when switching from sitting to standing position (dizziness postural)
- low levels of sodium in the blood, shown in a blood test (hyponatraemia)

Rare side effects (effects that occur in 1-10 in 10,000 users):
- seeing, hearing or feeling things that are not there (hallucinations)
- changes in sleeping pattern (sleep disorders)

Very rare side effects (effects that occur in less than 1 in 10,000 users):
- paranoia
- intestinal angioedema: a swelling in the gut presenting with symptoms like abdominal pain, nausea, vomiting and diarrhoea

Side effects of unknown frequency (frequency cannot be estimated from the available data):
- sudden involuntary muscle twitching (myoclonus)

If you experience any side effect, if any side effect gets worse, or if you experience a side effect not mentioned in this leaflet, consult your doctor.

Reporting side effects
You can report side effects to the Ministry of Health by following the link 'Reporting Side Effects of Drug Treatment' on the Ministry of Health home page (www.health.gov.il) which links to an online form for reporting side effects. You can also use this link: https://sideeffects.health.gov.il
Additionally, you can report to Novartis using the following e-mail address: safetydesk.israel@novartis.com.

5. How to store the medicine?

- Prevent poisoning! To prevent poisoning, keep this, and all other medicines, in a closed place, out of the reach and sight of children and/or infants. Do not induce vomiting unless explicitly instructed to do so by a doctor.
- Do not use the medicine after the expiry date (exp. date) which is stated on the carton and blister. The expiry date refers to the last day of that month.
- **Storage conditions:** Store below 30˚C. Protect from moisture. Do not use this medicine if the pack is damaged or shows signs of tampering.
- Do not throw away any medicines via wastewater (sewer). Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Additional information

- In addition to the active ingredients this medicine also contains –

Tablet core (50 mg, 100 mg, 200 mg)
Microcrystalline cellulose, low-substituted hydroxypropylcellulose, crospovidone, magnesium stearate, talc and silica colloidal anhydrous.

Tablet coating (50 mg, 200 mg)
Hypromellose, titanium dioxide (E171), polyethylene glycol 4000, talc, iron oxide red (E172) and iron oxide black (E172).

Tablet coating (100 mg)
Hypromellose, titanium dioxide (E171), polyethylene glycol 4000, talc, iron oxide yellow (E172) and iron oxide red (E172).

- **What the medicine looks like and contents of the pack -**
  Entresto 50 mg are violet-white oval film-coated tablets with “NVR” imprinted on one side of the tablet and “LZ” on the other side.
  Entresto 100 mg are pale yellow oval film-coated tablets with “NVR” imprinted on one side of the tablet and “L1” on the other side.
  Entresto 200 mg are light pink oval film-coated tablets with “NVR” imprinted on one side of the tablet and “L11” on the other side.

  The tablets are packaged in blisters.
  The packs contain 28 tablets (50 mg, 100 mg) or 56 tablets (100 mg and 200 mg).
  Not all pack sizes may be marketed.

Registration holder and importer’s name and address - Novartis Israel Ltd., P.O.B 7126, Tel Aviv, Israel.

This leaflet was revised in July 2025.

Registration number of the medicine in the Ministry of Health’s National Drug Registry:

- **Entresto 50 mg:** 154 97 34484
- **Entresto 100 mg:** 154 98 34485
- **Entresto 200 mg:** 154 99 34486