

The format of this leaflet was determined by the Ministry of Health and its content was checked and approved

#### **Patient Package Insert in accordance with the Pharmacists' Regulations (Preparations) – 1986**

The medicine is dispensed according to a physician's prescription only.

## Entresto™ 50 mg Film coated tablets

Each film coated tablet contains: 24 mg Sacubitril and 26 mg Valsartan as sodium salt complex

## Entresto™ 100 mg Film coated tablets

Each film coated tablet contains: 49 mg Sacubitril and 51 mg Valsartan as sodium salt complex

## Entresto™ 200 mg Film coated tablets

Each film coated tablet contains: 97 mg Sacubitril and 103 mg Valsartan as sodium salt complex

\*Inactive and allergenic ingredients in the medicinal product - see section 6 "Additional information".

**Read the entire leaflet carefully before using the medicine.** This leaflet contains concise information about the medicine. If you have any other questions, refer to the physician or the pharmacist.

This medicine has been prescribed for the treatment of your illness. Do not pass it on to others. It may harm them even if it seems to you that their illness is similar. The medicine is not intended for children and adolescents under the age of 18.

#### **1. What is the medicine intended for?**

Entresto is intended for heart failure patients (NYHA class 2-4) with a systolic problem. Entresto reduces cardiovascular mortality and hospitalisations due to heart failure to a much greater degree than angiotensin converting enzyme (ACE) inhibitors.

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.

Therapeutic group

Entresto is a medicine known as an angiotensin receptor neprilysin inhibitor. It dissociates into two active substances, sacubitril and valsartan.

#### **2. Before using the medicine**

##### **❌ Do not use the medicine if:**

- You are sensitive (allergic) to the active ingredients sacubitril, valsartan or to any of the other ingredients contained in the medicine (listed in section 6). If you think you may be allergic, talk to your doctor before taking Entresto.
- You are taking another type of medicine called an angiotensin converting enzyme (ACE) inhibitor (for example Enalapril, Lisinopril, Ramipril). ACE inhibitors are used to treat high blood pressure or heart failure. If you have been taking an ACE inhibitor, wait for 36 hours after taking the last dose before you start to take Entresto (see further on in this section).
- You have ever had a reaction called angioedema (swelling of the face, lips, tongue and/or throat, difficulties in breathing) when taking an ACE inhibitor or an angiotensin receptor blocker (ARB) (such as Valsartan, Telmisartan, Irbesartan).
- You have ever had angioedema when the reason why was not known or it was inherited.
- You are being treated with a blood pressure lowering medicine containing Aliskiren - in patients with diabetes or in patients with impaired kidney function (see further on in this section).
- You have severe liver disease.
- You are more than 3 months pregnant (it is also better to avoid this medicine in early pregnancy; see "Pregnancy and breast-feeding" section).
- You have hyperkalemia (high blood potassium level [ $>5.4$  mmol/l]) or your blood pressure is  $<100$  mmHg, as treatment should not be initiated.

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

#### **Special warnings regarding the use of the medicine**

**⚠ Before the treatment with Entresto, tell the physician**

- If you are being treated with an angiotensin receptor blocker (ARB) or Aliskiren (see "Do not use the medicine if").
- If you have ever had angioedema (see "Do not use the medicine if" and section 4 "Side Effects").
- If you have low blood pressure or are taking any other medicines that reduce your blood pressure (for example, a diuretic) 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.
- If you have severe kidney disease.
- If you are suffering from dehydration.
- If your kidney artery has narrowed.
- If you have liver disease.
- If you have blood pressure above 100 mmHg but less than 110 mmHg. Your physician may consider a lower starting dose. Your doctor may check the amount of potassium in your blood at regular intervals during Entresto treatment.

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

#### **⚠ Children and adolescents**

The medicine is not intended for children and adolescents under the age of 18 because it has not yet been studied in this age group.

**⚠ If you are taking or have recently taken other medicines including non-prescription medicines and food supplements, tell the physician or the pharmacist.** Especially inform the physician or the pharmacist if you are taking, have recently taken or might take any other medicines. 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:

- 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 to take Entresto (see "Do not use the medicine if").
- If you stop taking Entresto, wait 36 hours after taking your last dose of Entresto before starting treatment with an ACE inhibitor.
- Other medicines used to treat heart failure or lower blood pressure, such as angiotensin receptor blocker or Aliskiren (see "Do not use the medicine if").
- Some medicines known as statins that are used to lower high cholesterol levels (for example Atorvastatin).

- Sildenafil, a medicine used to treat erectile dysfunction or lung hypertension.
- Medicines that increase the amount of potassium in the blood. These include potassium supplements, salt substitutes containing potassium, potassium-sparing medicines and heparin.

- Painkillers of the type called non-steroidal anti-inflammatory medicines (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 regarding the use of the medicine").
- Lithium, a medicine used to treat some types of psychiatric disorders.
- Furosemide, a medicine belonging to the type known as diuretics, which are used to increase the amount of urine you produce.
- Nitroglycerine, a medicine to treat angina.
- Some types of antibiotic (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 applies to you, tell to your doctor or pharmacist before you take Entresto.**

#### **⚠ Using the medicine and food**

Entresto can be administered with or without food.

#### **⚠ Pregnancy and breast-feeding**

Pregnancy -

You must tell your doctor if you are (or might become) pregnant.

Your doctor will normally 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 must 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 any tools or machines.

#### **⚠ Important information about some ingredients of the medicine**

Each Entresto 50 mg tablet contains approximately 4 mg sodium.

Each Entresto 100 mg tablet contains approximately 8 mg sodium.

Each Entresto 200 mg tablet contains approximately 16 mg sodium.

#### **3. How should you use the medicine?**

Always use according to the physician's instructions. You should check with the physician or the pharmacist if you are unsure.

The dosage and treatment will be determined only by the physician. The recommended starting dose of Entresto is one tablet of 50 mg or 100 mg twice daily (one tablet in the morning and one tablet in the evening). Your doctor will decide your exact starting dose based on which medicines you have been taking previously. Your doctor will then adjust the dose 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).

Let your physician know if you have hyperkalemia (high blood potassium level [ $>5.4$  mmol/l]) or your blood pressure is  $<100$  mmHg, as treatment should not be initiated.

If you have blood pressure above 100 mmHg but less than 110 mmHg, your physician should consider a starting dose of 50 mg twice daily.

Elderly population -

If you are  $\geq$  75 years old, your physician should consider a starting dose of 50 mg Entresto twice daily.

Patients taking Entresto can develop low blood pressure (symptoms include dizziness, light-headedness), a high level of potassium in the blood (which would be detected when your doctor performed 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 your Entresto dose, or stop your Entresto treatment completely.

**Do not exceed the recommended dose.**

Swallow the medicine with a glass of water. You can take Entresto with or without food. Do not chew, crush, or divide.

The film coated tablet should not be broken or divided into parts.

#### **Tests and monitoring**

Your doctor may check the amount of potassium in your blood at regular intervals during Entresto treatment.

#### **If you accidentally have taken a higher dose**

If you have taken an overdose or if a child has accidentally swallowed the medicine, refer immediately to a physician or to a hospital emergency room and bring the package of the medicine with you. If you experience severe dizziness and/or fainting, tell a doctor as quickly as possible and lie down.

#### **If you forgot to take the medicine**

It is advisable to take your medicine at the same time each day.

If you forgot to take this medicine at the scheduled time, do not take a double dose to make up for a forgotten dose. You should take the next dose at the scheduled time and consult the physician. Persist with the treatment as recommended by the physician.

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

**If you stop taking the 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 the dose each time you take a medicine. Wear glasses if you need them.

If you have any other questions regarding the use of the medicine, consult the physician or the pharmacist.

#### **4. Side effects**

As with any medicine, use of Entresto may cause side effects in some of the users. Do not be alarmed by reading the list of side effects. You may not experience any of them.

#### **Some side effects may be serious.**

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

#### **Additional side effects**

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

**Very common side effects** (may affect more than 1 in 10 people):

- low blood pressure (dizziness, light-headedness)
- high level of potassium in the blood (shown in a blood test)
- decreased renal function (renal impairment)

**Common side effects** (may affect up to 1 in 10 people):

- cough
- dizziness
- diarrhoea
- low level of red blood cells (shown in a blood test)
- tiredness
- (acute) renal failure (severe kidney disorder)
- low level of potassium in the blood (shown in a blood test)
- headache
- fainting
- weakness
- feeling sick (nausea)
- low blood pressure (dizziness, light-headedness) when switching from sitting or lying to standing position
- gastritis (stomach pain, nausea)
- spinning sensation
- low level of sugar in blood (shown in a blood test)

**Uncommon side effects** (may affect up to 1 in 100 people):

- allergic reaction with rash and itching
- dizziness when switching from sitting to standing position (or vice versa)

#### **Reporting side effects**

Side effects can be reported to the Ministry of Health by clicking on the "Reporting side effects due to medicinal treatment" link on the homepage of the Ministry of Health website ([www.health.gov.il](http://www.health.gov.il)) or via the following link: <https://forms.gov.il/globaldata/getseque/getsequeance.aspx?formType=AdversEffectMedic@moh.gov.il>

If a side effect occurs, if any of the side effects gets worse, or when you suffer from a side effect not mentioned in the leaflet, you should consult the physician.

#### **5. How to store the medicine?**

- Avoid poisoning! This medicine and any other medicine should be kept in a closed place out of the sight and reach of children and/or infants in order to avoid poisoning. Do not induce vomiting without an explicit instruction from the physician.
- Do not use the medicine after the expiry date (exp. date) appearing on the package carton, and blister. The expiry date refers to the last day of that month.
- Store below 30°C.
- Protect from moisture.

- Store in the original package.
- Do not use the medicine if the package is damaged or shows signs of tampering.
- Do not throw away any medicines via wastewater. 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 the medicine also contains -

**Tablet core (50 mg, 100 mg, 200 mg)**  
Microcrystalline cellulose, low-substituted hydroxypropylcellulose, croscopovidone, magnesium stearate, talc and colloidal silicon dioxide.

**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 red (E172) and iron oxide yellow (E172).

- What does the medicine look like and what is the content of the package - Entresto 50 mg are violet-white oval tablets with "NVR" on one side and "LZ" on the other side. Entresto 100 mg are pale yellow oval tablets with "NVR" on one side and "L1" on the other side. Entresto 200 mg are light pink oval tablets with "NVR" on one side and "L11" on the other side. The tablets are supplied 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 address - Novartis Israel Ltd., 36 Shacham St., Petach-Tikva.
- Manufacturer and address - Novartis Pharma Stein AG, Stein, Switzerland
- or Novartis Farmap S.p.A., Torre Annunziata, Italy
- or Novartis Singapore Pharmaceutical Manufacturing Pte. Ltd., Singapore, Singapore
- For: Novartis Pharma AG, Basel, Switzerland.
- This leaflet was checked and approved by the Ministry of Health in August 2017.
- Registration number of the medicine in the National Drug Registry of the Ministry of Health:

**Entresto 50 mg:** 154 97 34484  
**Entresto 100 mg:** 154 98 34485  
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