Package leaflet: Information for the patient

Sacubitril/Valsartan Krka 24 mg/26 mg film-coated tablets
Sacubitril/Valsartan Krka 49 mg/51 mg film-coated tablets
Sacubitril/Valsartan Krka 97 mg/103 mg film-coated tablets
sacubitril/valsartan

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 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 Sacubitril/Valsartan Krka is and what it is used for

Sacubitril/Valsartan Krka is a heart medicine containing an angiotensin receptor neprilysin inhibitor. It delivers two active substances, sacubitril and valsartan.

Sacubitril/Valsartan Krka is used to treat a type of long-term heart failure in adults, children and adolescents (one year and older).

This type of 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. What you need to know before you take Sacubitril/Valsartan Krka

Do not take Sacubitril/Valsartan Krka
- if you are allergic to sacubitril, valsartan or any of the other ingredients of this medicine (listed in section 6).
- if 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 ACE inhibitor, wait for 36 hours after taking the last dose before you start to take Sacubitril/Valsartan Krka (see “Other medicines and Sacubitril/Valsartan Krka”).
- if you have ever had a reaction called angioedema (rapid 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).
- if you have a history of angioedema which is hereditary or for which the cause is unknown (idiopathic).
- if you have diabetes or impaired kidney function and you are being treated with a blood pressure lowering medicine containing aliskiren (see “Other medicines and Sacubitril/Valsartan Krka”).

- if you have severe liver disease.
- if you are more than 3 months pregnant (see "Pregnancy and breast-feeding").

If any of the above applies to you, do not take Sacubitril/Valsartan Krka and talk to your doctor.

Warnings and precautions
Talk to your doctor, pharmacist or nurse before and when taking Sacubitril/Valsartan Krka.
- if you are being treated with an angiotensin receptor blocker (ARB) or aliskiren (see "Do not take Sacubitril/Valsartan Krka").
- if you have ever had angioedema (see "Do not take Sacubitril/Valsartan Krka" and section 4 "Possible side effects").
- if you experience abdominal pain, nausea, vomiting or diarrhoea after taking Sacubitril/Valsartan Krka. Your doctor will decide on further treatment. Do not stop taking Sacubitril/Valsartan Krka on your own.
- if you have low blood pressure or are taking any other medicines that reduce your blood pressure (for example, a medicine that increases urine production (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 kidney disease.
- if you are suffering from dehydration.
- if your kidney artery has narrowed.
- if you have liver disease.
- if you experience hallucinations, paranoia or changes in sleeping pattern while taking Sacubitril/Valsartan Krka.
- if 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 applies to you, tell your doctor, pharmacist or nurse before you take Sacubitril/Valsartan Krka.

Your doctor may check the amount of potassium and sodium in your blood at regular intervals during Sacubitril/Valsartan Krka treatment. In addition, your doctor may check your blood pressure at start of treatment and when the doses are increased.

Children and adolescents
Do not give this medicine to children aged below 1 year because it has not been studied in this age group. This medicine is not suitable for children aged one year and older with a body weight below 40 kg because it may not be possible to take the correct dose with Sacubitril/Valsartan Krka tablets. Your doctor or pharmacist will check if there is a suitable alternative (granules) available, so that the correct dose can be taken.

Other medicines and Sacubitril/Valsartan Krka
Tell your doctor, pharmacist or nurse if you (or your child) 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 Sacubitril/Valsartan Krka 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 Sacubitril/Valsartan Krka (see "Do not take Sacubitril/Valsartan Krka"). If you stop taking Sacubitril/Valsartan Krka, wait 36 hours after taking your last dose of Sacubitril/Valsartan Krka 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 take Sacubitril/Valsartan Krka").
- some medicines known as statins 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. 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 "Warnings and precautions").
- lithium, a medicine used to treat some types of psychiatric illness.
- furosemide, a medicine belonging to the type known as diuretics, which are used to increase the amount of urine you produce.
- nitroglycerine, a medicine used to treat angina pectoris.
- some types of antibiotics (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 your doctor or pharmacist before you take Sacubitril/Valsartan Krka.

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.

Pregnancy
You must tell your doctor if you think that 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 Sacubitril/Valsartan Krka.

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
Sacubitril/Valsartan Krka 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 Sacubitril/Valsartan Krka affects you. If you feel dizzy or very tired while taking this medicine, do not drive a vehicle, cycle or use any tools or machines.

Sacubitril/Valsartan Krka contains sodium
This medicine contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially 'sodium free'.

3. How to take Sacubitril/Valsartan Krka

Always take this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

Adults
You will usually start by taking a 24 mg/26 mg or 49 mg/51 mg tablet 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 have been 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 97 mg/103 mg twice a day (one tablet in the morning and one tablet in the evening).

Children and adolescents (one year and older)
Your (or your child's) doctor will decide the starting dose based on body weight and other factors including previously taken medicines. The doctor will adjust the dose every 2-4 weeks until the best dose is found.

Sacubitril/Valsartan Krka should be given twice a day (one tablet in the morning and one tablet in the evening).

Sacubitril/Valsartan Krka film-coated tablets are not meant to be used in children who weigh less than 40 kg.
For these patients, your doctor or pharmacist will check if a suitable alternative (granules) is available.

Patients taking Sacubitril/Valsartan Krka can develop low blood pressure (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 the Sacubitril/Valsartan Krka dose, or stop Sacubitril/Valsartan Krka treatment completely.

Swallow the tablets with a glass of water. You can take Sacubitril/Valsartan Krka with or without food. Splitting or crushing of the tablets is not recommended. Sacubitril/Valsartan Krka tablets are film-coated in order to be protected from environmental influences and to enable you to swallow the tablet with more ease. The coating is not suitable for crushing.

If you take more Sacubitril/Valsartan Krka than you should
If you have accidentally taken too many Sacubitril/Valsartan Krka tablets, or if someone else has taken your tablets, contact your doctor immediately. If you experience severe dizziness and/or fainting, tell your doctor as quickly as possible and lie down.

If you forget to take Sacubitril/Valsartan Krka
It is advisable to take your medicine at the same time each day. However, if you forget to take a dose, you should simply take the next one at the scheduled time. Do not take a double dose to make up for a forgotten dose.

If you stop taking Sacubitril/Valsartan Krka
Stopping your treatment with Sacubitril/Valsartan Krka may cause your condition to get worse. Do not stop taking your medicine unless your doctor tells you to.

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.

Some side effects may be serious.
Stop taking Sacubitril/Valsartan Krka and seek immediate medical attention if you notice 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).

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

Very common (may affect more than 1 in 10 people)

- low blood pressure, which can cause symptoms of dizziness and light-headedness (hypotension)
- high level of potassium in the blood, shown in a blood test (hyperkalaemia)
- decreased kidney function (renal impairment)

Common (may affect up to 1 in 10 people)
- cough
- dizziness
- diarrhoea
- low level of red blood cells, shown in a blood test (anaemia)
- tiredness (fatigue)
- (acute) inability of the kidney to work properly (renal failure)
- low level of potassium in the blood, shown in a blood test (hypokalaemia)
- headache
- fainting (syncope)
- weakness (asthenia)
- feeling sick (nausea)
- low blood pressure (dizziness, light-headedness) when switching from sitting or lying to standing position
- gastritis (stomach pain, nausea)
- spinning sensation (vertigo)
- low level of sugar in the blood, shown in a blood test (hypoglycaemia)

Uncommon (may affect up to 1 in 100 people)
- allergic reaction with rash and itching (hypersensitivity)
- dizziness when switching from sitting to standing position (dizziness postural)
- low level of sodium in the blood, shown in a blood test (hyponatraemia)

Rare (may affect up to 1 in 1 000 people)
- seeing, hearing or feeling things that are not there (hallucinations)
- changes in sleeping pattern (sleep disorder)

Very rare (may affect up to 1 in 10 000 people)
- paranoia
- intestinal angioedema: a swelling in the gut presenting with symptoms like abdominal pain, nausea, vomiting and diarrhoea

Not known (frequency cannot be estimated from the available data)
- sudden involuntary muscle twitching (myoclonus).

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 HPRA Pharmacovigilance, Website: www.hpra.ie. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Sacubitril/Valsartan Krka

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 carton and blister after ‘EXP’. The expiry date refers to the last day of that month.

This medicine does not require any special temperature storage conditions.
Store in the original package in order to protect from moisture.

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 protect the environment.

6. Contents of the pack and other information

What Sacubitril/Valsartan Krka contains

- The active substances are sacubitril and valsartan.

  Sacubitril/Valsartan Krka 24 mg/26 mg film-coated tablets
  Each film-coated tablet contains sacubitril sodium equivalent to 24.3 mg sacubitril and valsartan disodium equivalent to 25.7 mg valsartan.

  Sacubitril/Valsartan Krka 49 mg/51 mg film-coated tablets
  Each film-coated tablet contains sacubitril sodium equivalent to 48.6 mg sacubitril and valsartan disodium equivalent to 51.4 mg valsartan.

  Sacubitril/Valsartan Krka 97 mg/103 mg film-coated tablets
  Each film-coated tablet contains sacubitril sodium equivalent to 97.2 mg sacubitril and valsartan disodium equivalent to 102.8 mg valsartan.

- The other ingredients in the tablet core are povidone, microcrystalline cellulose, talc, crospovidone, colloidal anhydrous silica and magnesium stearate.
- The other ingredients in the film coating are coating mixture (poly(vinyl alcohol), calcium carbonate, macrogol and talc), red iron oxide (E172) *[only for 24 mg/26 mg and 97 mg/103 mg]*, black iron oxide (E172) *[only for 24 mg/26 mg]* and yellow iron oxide (E172) *[only for 49 mg/51 mg]*.
  See section 2 "Sacubitril/Valsartan Krka contains sodium".

What Sacubitril/Valsartan Krka looks like and contents of the pack
Sacubitril/Valsartan Krka 24 mg/26 mg film-coated tablets
Light greyish pink, round, biconvex, film-coated tablet, marked with S3 on one side. Tablet dimension: diameter approx. 9 mm

Sacubitril/Valsartan Krka 49 mg/51 mg film-coated tablets
Yellow, round, biconvex, film-coated tablet, marked with S2 on one side. Tablet dimension: diameter approx. 9 mm

Sacubitril/Valsartan Krka 97 mg/103 mg film-coated tablets
Orangish pink, oval, biconvex, film-coated tablet, marked with S1 on one side. Tablet dimension: approx. 15 mm x 8 mm

Sacubitril/Valsartan Krka is available in packs containing
- 14, 20, 28, 56, 60, 168, 196 and 200 film-coated tablets, in blisters.
- 14, 28, 56, 168 and 196 film-coated tablets, in blisters, calendar pack.

Not all pack sizes may be marketed.

Marketing Authorisation Holder
KRKA, d.d., Novo mesto, Šmarješka cesta 6, 8501 Novo mesto, Slovenia

Manufacturer
KRKA, d.d., Novo mesto, Šmarješka cesta 6, 8501 Novo mesto, Slovenia
TAD Pharma GmbH, Heinz-Lohmann-Straße 5, 27472 Cuxhaven, Germany

This medicine is authorised in the Member States of the European Economic Area under the

following names:

Austria, Cyprus, Germany	Sacubitril/Valsartan TAD
Belgium, France	Sacubitril/Valsartan HCS
Denmark, Finland, Iceland, Ireland, Norway, Sweden	Sacubitril/Valsartan Krka
Italy	Sacubitril e Valsartan Krka
Portugal	Sacubitril + Valsartan TAD
Slovenia	Sakubitril/valsartan HCS

This leaflet was last revised in