Package leaflet: Information for the user

Sunitinib Krka 12.5 mg hard capsules
Sunitinib Krka 25 mg hard capsules
Sunitinib Krka 50 mg hard capsules
sunitinib

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

What is in this leaflet

1. What Sunitinib Krka is and what it is used for

Sunitinib Krka contains the active substance sunitinib, which is a protein kinase inhibitor. It is used to treat cancer by preventing the activity of a special group of proteins which are known to be involved in the growth and spread of cancer cells.

Sunitinib Krka is used to treat adults with the following types of cancer:

- Gastrointestinal stromal tumour (GIST), a type of cancer of the stomach and bowel, where imatinib (another anticancer medicine) no longer works or you cannot take imatinib.
- Metastatic renal cell carcinoma (MRCC), a type of kidney cancer that has spread to other parts of the body.
- Pancreatic neuroendocrine tumours (pNET) (tumours of the hormone-producing cells in the pancreas) that have progressed or cannot be removed with surgery.

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

2. What you need to know before you take Sunitinib Krka

Do not take Sunitinib Krka
- if you are allergic to sunitinib or any of the other ingredients of this medicine (listed in

section 6).

Warnings and precautions
Talk to your doctor before taking Sunitinib Krka:

- if you have high blood pressure. Sunitinib Krka can raise blood pressure. Your doctor may check your blood pressure during treatment with Sunitinib Krka, and you may be treated with medicines to reduce the blood pressure, if needed.

- if you have or have had blood disease, bleeding problems, or bruising. Treatment with Sunitinib Krka may lead to a higher risk of bleeding or lead to changes in the number of certain cells in the blood which may lead to anaemia or affect the ability of your blood to clot. If you are taking warfarin or acenocoumarole, medicines which thin the blood to prevent blood clots, there may be a greater risk of bleeding. Tell your doctor if you have any bleeding while on treatment with Sunitinib Krka.

- if you have heart problems. Sunitinib Krka can cause heart problems. Tell your doctor if you feel very tired, are short of breath, or have swollen feet and ankles.

- if you have abnormal heart rhythm changes. Sunitinib Krka can cause abnormality of your heart rhythm. Your doctor may obtain electrocardiograms to evaluate for these problems during your treatment with Sunitinib Krka. Tell your doctor if you feel dizzy, faint, or have abnormal heartbeats while taking Sunitinib Krka.

- if you have had a recent problem with blood clots in your veins and/or arteries (types of blood vessels), including stroke, heart attack, embolism, or thrombosis. Call your doctor immediately if you get symptoms such as chest pain or pressure, pain in your arms, back, neck or jaw, shortness of breath, numbness or weakness on 1 side of your body, trouble talking, headache, or dizziness while on treatment with Sunitinib Krka.

- if you have or have had an aneurysm (enlargement and weakening of a blood vessel wall) or a tear in a blood vessel wall.

- if you have or have had damage to the smallest blood vessels known as thrombotic microangiopathy (TMA). Tell your doctor if you develop fever, fatigue, tiredness, bruising, bleeding, swelling, confusion, vision loss, and seizures.

- if you have thyroid glands problems. Sunitinib Krka can cause thyroid gland problems. Tell your doctor if you get tired more easily, generally feel colder than other people, or your voice deepens whilst taking Sunitinib Krka. Your thyroid function should be checked before you take Sunitinib Krka and regularly while you are taking it. If your thyroid gland is not producing enough thyroid hormone, you may be treated with thyroid hormone replacement.

- if you have or have had pancreatic or gallbladder disorders. Tell your doctor if you develop any of the following signs and symptoms: pain in the area of the stomach (upper abdomen), nausea, vomiting, and fever. These may be caused by inflammation of the pancreas or gallbladder.

- if you have or have had liver problems. Tell your doctor if you develop any of the following signs and symptoms of liver problems during Sunitinib Krka treatment: itching, yellow eyes or skin, dark urine, and pain or discomfort in the right upper stomach area. Your doctor should do blood tests to check your liver function before and during treatment with Sunitinib Krka, and as clinically indicated.

- if you have or have had kidney problems. Your doctor will monitor your kidney function.

- if you are going to have surgery or if you had an operation recently. Sunitinib Krka may affect the way your wounds heal. You will usually be taken off Sunitinib Krka if you are having an operation. Your doctor will decide when to start Sunitinib Krka again.

- You may be advised to have a dental check-up before you start treatment with Sunitinib Krka:
  - if you have or have had pain in the mouth, teeth and/or jaw, swelling or sores inside the mouth, numbness or a feeling of heaviness in the jaw, or loosening of a tooth, tell your doctor and dentist immediately.
  - if you need to undergo an invasive dental treatment or dental surgery, tell your dentist that you are being treated with Sunitinib Krka in particular when you are also receiving or have received intravenous bisphosphonates. Bisphosphonates are medicines used to prevent bone complications that may have been given for another medical condition.

- if you have or have had skin and subcutaneous tissue disorders. While you are on this medicine "pyoderma gangrenosum" (painful skin ulceration) or “necrotising fasciitis” (rapidly spreading infection of the skin/soft tissue that may be life-threatening) may occur. Contact your doctor immediately if symptoms of infection occur around a skin injury, including fever, pain, redness, swelling, or drainage of pus or blood. This event is generally reversible after sunitinib discontinuation. Severe skin rashes (Stevens-Johnson syndrome, toxic epidermal necrolysis, erythema multiforme) have been reported with the use of sunitinib, appearing initially as reddish target-like spots or circular patches often with central blisters on the trunk. The rash may progress to widespread blistering or peeling of the skin and may be life-threatening. If you develop a rash or these skin symptoms, seek immediate advice from a doctor.

- if you have or have had seizures. Notify your doctor as soon as possible if you have high blood pressure, headache, or loss of sight.

- if you have diabetes. Blood sugar levels in diabetic patients should be checked regularly in order to assess if antidiabetic medicine’s dosage needs to be adjusted to minimise the risk of low blood sugar. Notify your doctor as soon as possible if you experience any signs and symptoms of low blood sugar (fatigue, palpitations, sweating, hunger and loss of consciousness).

Children and adolescents
Sunitinib Krka is not recommended for people aged under 18.

Other medicines and Sunitinib Krka
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines, including medicines obtained without a prescription and even those not prescribed.

Some medicines can affect the levels of Sunitinib Krka in your body. You should inform your doctor if you are taking medicines containing the following active substances:
- ketoconazole, itraconazole – used to treat fungal infections
- erythromycin, clarithromycin, rifampicin –used to treat infections
- ritonavir –used to treat HIV
- dexamethasone – a corticosteroid used for various conditions (such as allergic/breathing disorders or skin diseases)
- phenytoin, carbamazepine, phenobarbital – used to treat epilepsy and other neurological
- conditions
- herbal preparations containing St. John’s Wort (*Hypericum perforatum*) – used to treat

depression and anxiety.

Sunitinib Krka with food and drink
You should avoid drinking **grapefruit juice** while on treatment with Sunitinib 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.

If you might get pregnant, you should use a reliable method of contraception during treatment with Sunitinib Krka.

If you are breast-feeding, tell your doctor. You should not breast-feed during treatment with Sunitinib Krka.

Driving and using machines
If you experience dizziness or you feel unusually tired, take special care when driving or using machines.

Sunitinib Krka contains sodium
This medicine contains less than 1 mmol sodium (23 mg) per capsule, that is to say essentially 'sodium-free'.

3. How to take Sunitinib Krka

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

Your doctor will prescribe a dose that is right for you, depending on the type of cancer to be treated. If you are being treated for:
- GIST or MRCC: the usual dose is 50 mg once daily taken for 28 days (4 weeks), followed by 14 days (2 weeks) of rest (no medicine), in 6-week cycles.
- pNET: the usual dose is 37.5 mg once daily without a rest period.

Your doctor will determine the appropriate dose you need to take, as well as if and when you need to stop treatment with Sunitinib Krka.

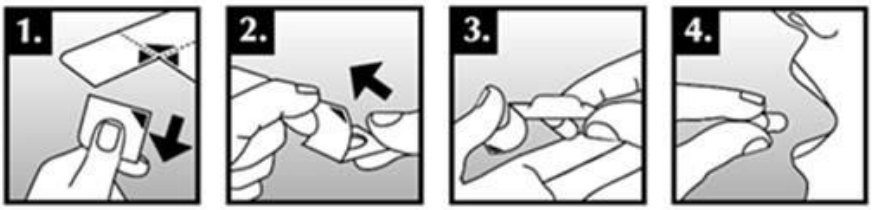
Sunitinib Krka can be taken with or without food.

Taking this medicine

Sunitinib capsules should not be pushed through the foil in the blister pack as this could cause damage to the capsule.
The capsule should be removed from the package by peeling off the foil from one separated blister cell.

To remove the capsule from the blister:
1. Hold the blister at the edges and separate one blister cell from the rest of the blister by

gently tearing along the perforations around it.
2. Pull up the edge of the foil and peel the foil off completely.
3. Tip the capsule out onto your hand.
4. Swallow the capsule whole.



If you take more Sunitinib Krka than you should
If you have accidentally taken too many capsules, talk to your doctor straight away. You may require medical attention.

If you forget to take Sunitinib Krka
Do not take a double dose to make up for a forgotten dose.

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.

You must immediately contact your doctor if you experience any of those serious side effects (see also section 2, "What you need to know before you take Sunitinib Krka):

- heart problems. Tell your doctor if you feel very tired, are short of breath, or have swollen feet and ankles. These may be symptoms of heart problems that may include heart failure and heart muscle problems cardiomyopathy).

- lung or breathing problems. Tell your doctor if you develop cough, chest pain, sudden onset of shortness of breath, or coughing up blood. These may be symptoms of a condition called pulmonary embolism that occurs when blood clots travel to your lungs.

- kidney disorders. Tell your doctor if you experience altered frequency or absence of urination which may be symptoms of kidney failure.

- bleeding. Tell your doctor if you have any of these symptoms or a serious bleeding problem during treatment with Sunitinib Krka: painful, swollen stomach (abdomen); vomiting blood; black, sticky stools; bloody urine; headache or change in your mental status; coughing up of blood or bloody sputum from the lungs or airway.

- tumour destruction leading to hole in the intestine. Tell your doctor if you have severe abdominal pain, fever, nausea, vomiting, blood in your stool, or changes in bowel habits.

Other side effects with Sunitinib Krka may include:

Very common side effects (may affect more than 1 in 10 people)
- reduction in the number of platelets, red blood cells and/or white blood cells (e.g. neutrophils)
- shortness of breath
- high blood pressure
- extreme tiredness, loss of strength
- swelling caused by fluid under the skin and around the eye, deep allergic rash
- mouth pain/irritation, mouth sores/inflammation/dryness, taste disturbances, upset stomach, nausea, vomiting, diarrhoea, constipation, abdominal pain/swelling, loss/decrease of appetite
- decreased activity of thyroid gland (hypothyroidism)
- dizziness
- headache
- nose bleeding
- back pain, joint pain
- pain in arms and legs
- yellow skin/skin discoloration, excess pigmentation of the skin, hair colour change, rash on the palms of the hands and soles of the feet, rash, dryness of the skin
- cough
- fever
- difficulty in falling asleep

Common side effects (may affect up to 1 in 10 people)
- blood clots in the blood vessels
- deficiency of blood supply to the heart muscle, due to obstruction or constriction of the coronary arteries
- chest pain
- decrease in the amount of blood pumped by the heart
- fluid retention including around the lungs
- infections
- complication of severe infection (infection is present in the bloodstream) that can lead to tissue damage, organ failure, and death
- decreased blood sugar level (see section 2, “What you need to know before you take Sunitinib Krka”)
- loss of protein in the urine sometimes resulting in swelling
- influenza-like syndrome
- abnormal blood tests including pancreatic and liver enzymes
- high level of uric acid in the blood
- haemorrhoids, pain in the rectum, gingival bleeding, difficulty in swallowing or inability to swallow
- burning or painful sensation in the tongue, inflammation of the digestive tract lining, excessive gas in the stomach or intestine
- weight loss
- musculoskeletal pain (pain in muscles and bones), muscular weakness, muscular fatigue, muscle pain, muscle spasms
- nasal dryness, congested nose
- excessive tear flow
- abnormal sensation of the skin, itching, flaking and inflammation of the skin, blisters, acne, nail discolouration, hair loss
- abnormal sensations in extremities
- abnormally decreased/increased sensitivity, particularly to touch
- acid heartburn
- dehydration
- hot flushes
- abnormally coloured urine

- depression
- chills

Uncommon side effects (may affect up to 1 in 100 people)
- life-threatening infection of the soft tissue including the ano-genital region (see section 2, "What you need to know before you take Sunitinib Krka")
- stroke
- heart attack caused by an interrupted or decreased blood supply to the heart
- changes in the electrical activity or abnormal rhythm of the heart
- fluid around the heart (pericardial effusion)
- liver failure
- pain in the stomach (abdomen) caused by inflammation of the pancreas
- tumour destruction leading to hole in the intestine (perforation)
- inflammation (swelling and redness) of the gallbladder with or without associated gallstones
- abnormal tube like passage from one normal body cavity to another body cavity or the skin
- pain in the mouth, teeth and/or jaw, swelling or sores inside the mouth, numbness or a feeling of heaviness in the jaw, or loosening of a tooth. These could be signs and symptoms of bone damage in the jaw (osteonecrosis), see section 2, "What you need to know before you take Sunitinib Krka
- overproduction of thyroid hormones which increases the amount of energy the body uses at rest
- problems with wound healing after surgery
- increased blood level of enzyme (creatine phosphokinase) from muscle
- excessive reaction to an allergen including hay fever, skin rash, itchy skin, hives, swelling of body parts, and trouble breathing
- inflammation of the colon (colitis, colitis ischaemic)

Rare side effects (may affect up to 1 in 1,000 people)
- severe reaction of the skin and/or mucous membranes (Stevens-Johnson syndrome, toxic epidermal necrolysis, erythema multiforme)
- tumour lysis syndrome (TLS) – TLS consists of a group of metabolic complications that can occur during treatment of cancer. These complications are caused by the break-down products of dying cancer cells and may include the following: nausea, shortness of breath, irregular heartbeat, muscular cramps, seizure, clouding of urine and tiredness associated with abnormal laboratory test results (high potassium, uric acid and phosphorous levels and low calcium levels in the blood) that can lead to changes in kidney function and acute renal failure
- abnormal muscle breakdown which can lead to kidney problems (rhabdomyolysis)
- abnormal changes in the brain that can cause a collection of symptoms including headache, confusion, seizures, and vision loss (reversible posterior leukoencephalopathy syndrome)
- painful skin ulceration (pyoderma gangrenosum)
- inflammation of the liver (hepatitis)
- inflammation of the thyroid gland
- damage to the smallest blood vessels known as thrombotic microangiopathy (TMA)

Not known side effects (frequency cannot be estimated from available data):
- an enlargement and weakening of a blood vessel wall or a tear in a blood vessel wall (aneurysms and artery dissections)

Reporting of side effects
If you get any side effects, talk to your doctor. 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 Sunitinib 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, container and blister foil after 'EXP'. The expiry date refers to the last day of that month.

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

Do not use this medicine if you notice that the pack is damaged or shows signs of tampering.

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 Sunitinib Krka contains

[Sunitinib Krka 12.5 mg hard capsules]
The active substance is sunitinib. Each hard capsule contains sunitinib malate equivalent to 12.5 mg sunitinib.
The other ingredients are:
- *Capsule content*: povidone, microcrystalline cellulose, croscarmellose sodium (see section 2, "Sunitinib Krka contains sodium"), magnesium stereate;
- *Capsule shell*: gelatin, titanium dioxide (E171), red iron oxide (E172), yellow iron oxide (E172).
- *Printing ink:* shellac, titanium dioxide (E171), propylene glycol.

[Sunitinib Krka 25 mg hard capsules]
The active substance is sunitinib. Each capsule contains sunitinib malate equivalent to 25 mg sunitinib.
The other ingredients are:
- *Capsule content*: povidone, microcrystalline cellulose, croscarmellose sodium (see section 2, "Sunitinib Krka contains sodium"), magnesium stereate;
- *Capsule shell*: gelatin, titanium dioxide (E171), red iron oxide (E172), yellow iron oxide (E172), black iron oxide (E172).
- *Printing ink:* shellac, titanium dioxide (E171), propylene glycol.

[Sunitinib Krka 50 mg hard capsules]
The active substance is sunitinib. Each hard capsule contains sunitinib malate equivalent to 50 mg sunitinib.
The other ingredients are:
- *Capsule content*: povidone, microcrystalline cellulose, croscarmellose sodium (see

section 2, “Sunitinib Krka contains sodium”), magnesium stereate;
- *Capsule shell*: gelatin, titanium dioxide (E171), red iron oxide (E172), yellow iron oxide (E172), black iron oxide (E172).
- *Printing ink:* shellac, black iron oxide (E172), propylene glycol.

What Sunitinib Krka looks like and contents of the pack

[Sunitinib Krka 12.5 mg hard capsules]
Sunitinib Krka 12.5 mg: hard gelatine capsule (capsule) with orange cap and orange body, printed with white imprint “SNB” and “12.5” on the body. The capsule is filled with orange powder. Capsule size: 4 (length of approximately 14 mm).

[Sunitinib Krka 25 mg hard capsules]
Sunitinib Krka 25 mg: hard gelatine capsule (capsule) with caramel (light brown) cap and orange body, printed with white imprint “SNB” and “25” on the body. The capsule is filled with orange powder. Capsule size: 3 (length of approximately 16 mm).

[Sunitinib Krka 50 mg hard capsules]
Sunitinib Krka 50 mg: hard gelatine capsule (capsule) with caramel cap and caramel body (light brown), printed with black imprint “SNB” and “50” on the body. The capsule is filled with orange powder. Capsule size: 1EL (elongated; length of approximately 20 mm).

It is available in plastic containers with desiccant of 30 hard capsules and in unit dose peel off blisters with desiccant containing 7 x 1, 10 x 1, 14 x 1, 20 x 1, 21 x 1, 28 x 1 or 30 x 1 hard capsules in a carton.

Not all pack sizes may be marketed.

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

Manufacturer(s):
KRKA, d.d. Novo mesto, Šmarješka cesta 6, 8501 Novo mesto Slovenia
KRKA – FARMA d.o.o., V. Holjevca 20/E, 10450 Jastrebarsko, Croatia
Synthon BV, Microweg 22, 6545CM Nijmegen, Netherlands
Synthon Hispania S.L., Castello 1, Poligono Las Salinas, 08830 Sant Boi de Llobregat, Spain
Synthon s.r.o., Brněnská 597/32, 678 01 Blansko, Czech Republic

This medicinal product is authorised in the Member States of the EEA under the following names:

Name of the Member State	**Name of the medicinal product**
Bulgaria	Сунитиниб Крка
Belgium, Croatia, Czech Republic, Denmark, Estonia, Finland, Hungary, Iceland, Ireland, Latvia, Lithuania, Norway, Poland, Slovakia, Slovenia, Sweden,	Sunitinib Krka
France	SUNITINIB KRKA

1.3.1	Sunitinib
SPC, Labeling and Package Leaflet	IE-Ireland

Netherland	Sunitinib HCS

This leaflet was last revised in