Package leaflet: Information for the user

Dasatinib Krka 20 mg film-coated tablets
Dasatinib Krka 50 mg film-coated tablets
Dasatinib Krka 70 mg film-coated tablets
Dasatinib Krka 80 mg film-coated tablets
Dasatinib Krka 100 mg film-coated tablets
Dasatinib Krka 140 mg film-coated tablets

dasatinib

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 Dasatinib Krka is and what it is used for
2. What you need to know before you take Dasatinib Krka
3. How to take Dasatinib Krka
4. Possible side effects
5. How to store Dasatinib Krka
6. Contents of the pack and other information

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

Dasatinib Krka contains the active substance dasatinib.
This medicine is used to treat Philadelphia chromosome positive (Ph+) acute lymphoblastic leukaemia (ALL) in adults, adolescents and children at least 1 year of age. In people with ALL, white cells called lymphocytes multiply too quickly and live too long. Dasatinib Krka inhibits the growth of these leukaemic cells.

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

Dasatinib which is contained in Dasatinib Krka is also authorised to treat other conditions which are not mentioned in this leaflet. Ask your doctor or pharmacist if you have further questions.

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

Do not take Dasatinib Krka
- if you are allergic to dasatinib or any of the other ingredients of this medicine (listed in section 6).

If you could be allergic, ask your doctor for advice.

Warnings and precautions
Talk to your doctor or pharmacist before using Dasatinib Krka
- if you are taking medicines to thin the blood or prevent clots (see "Other medicines and Dasatinib Krka")
- if you have a liver or heart problem, or used to have one

- if you start having difficulty breathing, chest pain, or a cough when taking Dasatinib Krka: this may be a sign of fluid retention in the lungs or chest (which can be more common in patients aged 65 years and older), or due to changes in the blood vessels supplying the lungs
- if you have ever had or might now have a hepatitis B infection. This is because Dasatinib Krka could cause hepatitis B to become active again, which can be fatal in some cases. Patients will be carefully checked by their doctor for signs of this infection before treatment is started
- if you experience bruising, bleeding, fever, fatigue and confusion when taking Dasatinib Krka, contact your doctor. This may be a sign of damage to blood vessels known as thrombotic microangiopathy (TMA).

Your doctor will regularly monitor your condition to check whether Dasatinib Krka is having the desired effect. You will also have blood tests regularly while you are taking Dasatinib Krka.

Children and adolescents
Do not give this medicine to children younger than one year of age . There is limited experience with the use of Dasatinib Krka in this age group. Bone growth and development will be closely monitored in children taking Dasatinib Krka.

Other medicines and Dasatinib Krka
Tell your doctor if you are taking, have recently taken or might take any other medicines.

Dasatinib Krka is mainly handled by the liver. Certain medicines may interfere with the effect of Dasatinib Krka when taken together.

These medicines are not to be used with Dasatinib Krka:
- ketoconazole, itraconazole - these are antifungal medicines
- erythromycin, clarithromycin, telithromycin - these are antibiotics
- ritonavir - this is an antiviral medicine
- phenytoin, carbamazepine, phenobarbital - these are treaments for epilepsy
- rifampicin - this is a treatment for tuberculosis
- famotidine, omeprazole - these are medicines that block stomach acids
- St. John's wort - a herbal preparation obtained without a prescription, used to treat depression and other conditions (also known as *Hypericum perforatum*)

Do not take medicines that neutralise stomach acids (antacids such as aluminium hydroxide or magnesium hydroxide) in the 2 hours before or 2 hours after taking Dasatinib Krka.

Tell your doctor if you are taking medicines to thin the blood or prevent clots.

Dasatinib Krka with food and drink
Do not take Dasatinib Krka with grapefruit or grapefruit juice.

Pregnancy and breast-feeding
If you are pregnant or think you may be pregnant, tell your doctor immediately. Dasatinib Krka is not to be used during pregnancy unless clearly necessary. Your doctor will discuss with you the potential risk of taking Dasatinib Krka during pregnancy.
Both men and women taking Dasatinib Krka will be advised to use effective contraception during treatment.

If you are breast-feeding, tell your doctor. You should stop breast-feeding while you are taking Dasatinib Krka.

Driving and using machines
Take special care when driving or using machines in case you experience side effects such as dizziness and blurred vision.

Dasatinib Krka contains lactose and sodium
If you have been told by your doctor that you have an intolerance to some sugars, talk to your doctor before taking this medicine.

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

3 How to take Dasatinib Krka

Dasatinib Krka will only be prescribed to you by a doctor with experience in treating leukaemia. Always take this medicine exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure. Dasatinib Krka is prescribed for adults and children at least 1 year of age.

The starting dose recommended for adult patients with Ph+ ALL is 140 mg once a day.

Dosing for children with Ph+ ALL is on the basis of body weight.
Dasatinib is administered orally once daily in the form of either dasatinib tablets or dasatinib powder for oral suspension. Dasatinib tablets are not recommended for patients weighing less than 10 kg. The powder for oral suspension should be used for patients weighing less than 10 kg and patients who cannot swallow tablets. A change in dose may occur when switching between formulations (i.e., tablets and powder for oral suspension), so you should not switch from one to the other. Your doctor will decide the right formulation and dose based on your weight, any side effects and response to treatment. The starting dose of Dasatinib Krka for children is calculated by body weight as shown below:

Body Weight (kg)[a]	**Daily Dose (mg)**
10 to less than 20 kg	40 mg
20 to less than 30 kg	60 mg
30 to less than 45 kg	70 mg
at least 45 kg	100 mg

[a] The tablet is not recommended for patients weighing less than 10 kg; the powder for oral suspension should be used for these patients.

There is no dose recommendation for Dasatinib Krka with children under 1 year of age.

Depending on how you respond to the treatment, your doctor may suggest a higher or lower dose, or even stopping treatment briefly. For higher or lower doses, you may need to take combinations of the different tablet strengths.

How to take Dasatinib Krka
Take your tablets at the same time every day. Swallow the tablets whole. Do not crush, cut or chew them. Do not take dispersed tablets. You cannot be sure you will receive the correct dose if you crush, cut, chew or disperse the tablets. Dasatinib Krka tablets can be taken with or without a meal.

Special handling instructions for Dasatinib Krka
It is unlikely that the Dasatinib Krka tablets will get broken. But if they do, persons other than the patient should use gloves when handling Dasatinib Krka.

How long to take Dasatinib Krka
Take Dasatinib Krka daily until your doctor tells you to stop. Make sure you take Dasatinib Krka for as long as it is prescribed.

If you take more Dasatinib Krka than you should

If you have accidentally taken too many tablets, talk to your doctor immediately. You may require medical attention.

If you forget to take Dasatinib Krka
Do not take a double dose to make up for a forgotten tablet. Take the next scheduled dose at the regular time.

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.

The following can all be signs of serious side effects:
- if you have chest pain, difficulty breathing, coughing and fainting
- if you experience unexpected bleeding or bruising without having an injury
- if you find blood in your vomit, stools or urine, or have black stools
- if you get signs of infections such as fever, severe chills
- if you get fever, sore mouth or throat, blistering or peeling of your skin and/or mucous membranes

Contact your doctor immediately if you notice any of the above.

Very common side effects (may affect more than 1 in 10 people)
- **Infections** (including bacterial, viral and fungal)
- **Heart and lungs**: shortness of breath
- **Digestive problems**: diarrhoea, feeling or being sick (nausea, vomiting)
- **Skin, hair, eye, general**: skin rash, fever, swelling around the face, hands and feet, headache, feeling tired or weak, bleeding
- **Pain**: pain in the muscles (during or after discontinuing treatment), tummy (abdominal) pain
- **Tests may show**: low blood platelet count, low white blood cells count (neutropaenia), anaemia, fluid around the lungs

Common side effects (may affect up to 1 in 10 people)
- **Infections**: pneumonia, herpes virus infection (including cytomegalovirus - CMV), upper respiratory tract infection, serious infection of the blood or tissues (including uncommon cases with fatal outcomes)
- **Heart and lungs**: palpitations, irregular heartbeat, congestive heart failure, weak heart muscle, high blood pressure, increased blood pressure in the lungs, cough
- **Digestive problems**: appetite disturbances, taste disturbance, bloated or distended tummy (abdomen), inflammation of the colon, constipation, heartburn, mouth ulceration, weight increase, weight decrease, gastritis
- **Skin, hair, eye, general**: skin tingling, itching, dry skin, acne, inflammation of the skin, persistent noise in ears, hair loss, excessive perspiration, visual disorder (including blurred vision and disturbed vision), dry eye, bruise, depression, insomnia, flushing, dizziness, contusion (bruising), anorexia, somnolence, generalised oedema
- **Pain**: pain in joints, muscular weakness, chest pain, pain around hands and feet, chills, stiffness in muscles and joints, muscle spasm
- **Tests may show**: fluid around the heart, fluid in the lungs, arrhythmia, febrile neutropaenia, gastrointestinal bleeding, high uric acid levels in the blood

Uncommon side effects (may affect up to 1 in 100 people)
- **Heart and lungs**: heart attack (including fatal outcome), inflammation of the lining (fibrous sack) surrounding the heart, irregular heartbeat, chest pain due to lack of blood supply to the heart (angina), low blood pressure, narrowing of airway that may cause breathing difficulties, asthma, increased blood pressure in the arteries (blood vessels) of the lungs

- **Digestive problems**: inflammation of the pancreas, peptic ulcer, inflammation of the food pipe, swollen tummy (abdomen), tear in the skin of the anal canal, difficulty in swallowing, inflammation of the gallbladder, blockage of bile ducts, gastro-oesophageal reflux (a condition where acid and other stomach contents come back up into the throat)
- **Skin, hair, eye, general**: allergic reaction including tender, red lumps on the skin (erythema nodosum), anxiety, confusion, mood swings, lower sexual drive, fainting, tremor, inflammation of the eye which causes redness or pain, a skin disease characterized by tender, red, well-defined blotches with the sudden onset of fever and raised white blood cell count (neutrophilic dermatosis), loss of hearing, sensitivity to light, visual impairment, increased eye tearing, disturbance in skin colour, inflammation of fatty tissue under the skin, skin ulcer, blistering of the skin, nail disorder, hair disorder, hand-foot disorder, renal failure, urinary frequency, breast enlargement in men, menstrual disorder, general weakness and discomfort, low thyroid function, losing balance while walking, osteonecrosis (a disease of reduced blood flow to the bones, which can cause bone loss and bone death), arthritis, skin swelling anywhere in the body
- **Pain**: inflammation of vein which can cause redness, tenderness and swelling, inflammation of the tendon
- **Brain**: loss of memory
- **Tests may show**: abnormal blood test results and possibly impaired kidney function caused by the waste products of the dying tumour (tumour lysis syndrome), low levels of albumin in the blood, low levels of lymphocytes (a type of white blood cell) in the blood, high level of cholesterol in the blood, swollen lymph nodes, bleeding in the brain, irregularity of the electrical activity of the heart, enlarged heart, inflammation of the liver, protein in the urine, raised creatine phosphokinase (an enzyme mainly found in the heart, brain and skeletal muscles), raised troponin (an enzyme mainly found in the heart and skeletal muscles), raised gamma-glutamyltransferase (an enzyme mainly found in the liver), milky-appearing fluid around the lungs (chylothorax)

Rare side effects (may affect up to 1 in 1,000 people)
- **Heart and lungs**: enlargement of the right ventricle in the heart, inflammation of the heart muscle, collection of conditions resulting from blockage of blood supply to the heart muscle (acute coronary syndrome), cardiac arrest (stopping of blood flow from the heart), coronary (heart) artery disease, inflammation of the tissue covering the heart and lungs, blood clots, blood clots in the lungs
- **Digestive problems**: loss of vital nutrients such as protein from your digestive tract, bowel obstruction, anal fistula (an abnormal opening from the anus to the skin around the anus), impairment of kidney function, diabetes
- **Skin, hair, eye, general**: convulsion, inflammation of the optic nerve that may cause a complete or partial loss of vision, blue-purple mottling of the skin, abnormally high thyroid function, inflammation of the thyroid gland, ataxia (a condition associated with lack of muscular coordination), difficulty walking, miscarriage, inflammation of the skin blood vessels, skin fibrosis
- **Brain**: stroke, temporary episode of neurologic dysfunction caused by loss of blood flow, facial nerve paralysis, dementia
- **Immune system**: severe allergic reaction
- **Musculoskeletal and connective tissue**: delayed fusion of the rounded ends that form joints (epiphyses); slower or delayed growth

Other side effects that have been reported with frequency **not known** (cannot be estimated from the available data)
- Inflammation of the lungs
- Bleeding in the stomach or bowels that can cause death
- Recurrence (reactivation) of hepatitis B infection when you have had hepatitis B in the past (a liver infection)
- A reaction with fever, blisters on the skin, and ulceration of the mucous membranes
- Disease of the kidneys with symptoms including oedema and abnormal laboratory test results such as protein in the urine and low protein level in the blood

- Damage to blood vessels known as thrombotic microangiopathy (TMA), including decreased red blood cell count, decreased platelets, and formation of blood clots

Your doctor will check for some of these effects during your treatment.

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. 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 Dasatinib 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 blister or carton after EXP. The expiry date refers to the last day of that month.

This medicine 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 protect the environment.

6. Contents of the pack and other information

What Dasatinib Krka contains
- The active substance is dasatinib. Each film-coated tablet contains 20 mg, 50 mg, 70 mg, 80 mg, 100 mg or 140 mg dasatinib.
- The other ingredients are:
  Tablet core: lactose monohydrate (200); microcrystalline cellulose (101 and 102); croscarmellose sodium; hydroxypropylcellulose (MW 80,000); magnesium stearate.
  Film-coating: lactose monohydrate; hypromellose (15 mPas); titanium dioxide (E171); triacetin.
  See section 2 "Dasatinib Krka contains lactose and sodium".

What Dasatinib Krka looks like and contents of the pack
Dasatinib Krka 20 mg: the film-coated tablet (tablet) is white to off-white, biconvex, round with a diameter of approximately 5.6 mm, with “D7SB” debossed on one side and “20” on the other side.

Dasatinib Krka 50 mg: the film-coated tablet (tablet) is white to off-white, biconvex, oval with a length of approximately 11.0 mm and a width of approximately 6.0 mm, with “D7SB” debossed on one side and “50” on the other side.

Dasatinib Krka 70 mg: the film-coated tablet (tablet) is white to off-white, biconvex, round with a diameter of approximately 9.1 mm, with “D7SB” debossed on one side and “70” on the other side.

Dasatinib Krka 80 mg: the film-coated tablet (tablet) is white to off-white, biconvex, triangular with a length of approximately 10.4 mm and a width of approximately 10.6 mm, with “D7SB” debossed on one side and “80” on the other side.

Dasatinib Krka 100 mg: the film-coated tablet (tablet) is white to off-white, biconvex, oval with a length of approximately 15.1 mm and a width of approximately 7.1 mm, with “D7SB” debossed on one side and “100” on the other side.

Dasatinib Krka 140 mg: the film-coated tablet (tablet) is white to off-white, biconvex, round with a

diameter of approximately 11.7 mm, with “D7SB” debossed on one side and “140” on the other side.

Dasatinib Krka of all strengths is available in boxes containing:
- 30 or 60 film-coated tablets, in non-perforated blisters.

Not all pack sizes may be marketed.

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

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

Name of the member state	**Name of the medicine**
Netherlands, Belgium, Czech Republic, Denmark, Finland, France, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Norway, Poland, Portugal, Romania, Slovak Republic, Slovenia, Schweden	Dasatinib Krka
Austria	Dasatinib HCS
Bulgaria	Дазатиниб Krka

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