PATIENT INFORMATION LEAFLET

SCHEDULING STATUS: S4

SPRYCEL® 20 mg tablets

SPRYCEL® 50 mg tablets

SPRYCEL® 70 mg tablets

SPRYCEL® 100 mg tablets

Dasatinib

SPRYCEL® 20 mg contains sugar (lactose) 27,0 mg per tablet

SPRYCEL® 50 mg contains sugar (lactose) 67,5 mg per tablet

SPRYCEL® 70 mg contains sugar (lactose) 94,5 mg per tablet

SPRYCEL® 100 mg contains sugar (lactose) 135,0 mg per tablet

Read all of this leaflet carefully before you start taking SPRYCEL

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor, pharmacist, nurse or other health care provider.
- SPRYCEL has been prescribed for you personally and you should not share your medicine with other people. It may harm them, even if their symptoms are the same as yours.

What is in this leaflet

1. What SPRYCEL is and what it is used for

SPRYCEL tablets contain 20, 50, 70 or 100 mg dasatinib.

SPRYCEL (dasatinib) is used to treat adults who have chronic myeloid leukaemia (CML) or have Philadelphia chromosome positive or Ph+ acute lymphoblastic leukaemia (ALL).

2. What you need to know before you take SPRYCEL

Do not take SPRYCEL:

- If you are hypersensitive (allergic) to dasatinib or any of the other ingredients of SPRYCEL.
- If you are using H_2 blockers or proton pump inhibitors with SPRYCEL is not recommended.

Warnings and precautions

Take special care with SPRYCEL:

- if you are taking **medicines to thin the blood** or prevent clots (**see Other medicines and SPRYCEL**)
- if you have problems with your immune system
- if you have a liver problem
- if you have heart problems, including a condition called congenital long QT syndrome
- if you have low potassium or low magnesium levels in your blood
- if you start having difficulty breathing, chest pain, or a cough when taking SPRYCEL: this may be a sign of fluid retention in the lungs or chest (which can be more common in patients aged 65 years or older), or due to changes in the blood vessels supplying the lungs.
- if you have ever had or might now have hepatitis B infection. This is because SPRYCEL 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 SPRYCEL, 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 SPRYCEL is having the desired effect. You will also have blood tests regularly while you are taking SPRYCEL.

Children and adolescents

SPRYCEL has not been studied in children

Other medicines and SPRYCEL

Always tell your health care provider if you are taking any other medicines. (This includes all complementary or traditional medicines).

SPRYCEL is eliminated from your body through the liver. The use of certain other medicines may alter the levels of SPRYCEL in your bloodstream. Likewise, levels of other medicines in your bloodstream can be affected by SPRYCEL. Such changes can increase the side effects or reduce the activity of the medicines you are taking, including SPRYCEL.

- Medicines that increase the amount of SPRYCEL in your bloodstream are:
  - ketoconazole, itraconazole – these are antifungal medicines
  - ritonavir, atazanavir sulfate, indinavir, nelfinavir, saquinavir – these are antiviral medicine
  - telithromycin, erythromycin and clarithromycin – these are antibiotics
- Medicines that decrease the amount of SPRYCEL in your bloodstream are:

  Dexamethasone – a corticosteroid medication
  - phenytoin, carbamazepine, phenobarbital – these are treatments for epilepsy
  - rifampicin – this is treatment for tuberculosis
  - St. John' Wort - a herbal preparation obtained without a prescription, used to treat depression and other conditions
- Medicines whose blood levels might be altered by SPRYCEL are ciclosporin, alfentanil, fentanyl, pimozide, sirolimus, tacrolimus and ergotamine.

SPRYCEL is best absorbed from your stomach into your bloodstream in the presence of stomach acid. You should avoid taking medicines that reduce stomach acid such as cimetidine, famotidine, ranitidine, omeprazole, pantoprazole sodium, esomeprazole, rabeprazole, or lansoprazole while taking SPRYCEL. Medicines that neutralise stomach acid, such as aluminium hydroxide/magnesium hydroxide, calcium carbonate, or calcium carbonate and magnesium hydroxide may be taken up to 2 hours before or 2 hours after SPRYCEL.

Since SPRYCEL therapy may cause bleeding, tell your healthcare provider if you are using blood thinners, such as warfarin or aspirin.

SPRYCEL with food and drink and alcohol

Do not drink grapefruit juice when you are taking SPRYCEL

Pregnancy and breastfeeding and fertility

Women who are pregnant or planning to become pregnant should not take SPRYCEL.

- SPRYCEL may harm the baby when given to a pregnant woman. Women should avoid becoming pregnant while undergoing treatment with SPRYCEL.

If you are pregnant or breastfeeding, think you may be pregnant or are planning to have a baby, please consult your doctor, pharmacist or other health care provider for advice before taking this medicine.

- It is not known if SPRYCEL can pass into your breast milk or if it can harm your baby. Do not breastfeed if you are taking SPRYCEL.
- Sexually active men who take SPRYCEL, are advised to use a condom to avoid pregnancy in their partner.

Driving and using machines

No studies of the effects on the ability to drive and use machines when taking SPRYCEL have been performed.

It is not always possible to predict to what extent SPRYCEL may interfere with the daily activities of a patient. Patients should ensure that they do not engage in the following activities (e.g driving, riding, flying, sailing, operating machines/equipment) until they are aware of the measure to which SPRYCEL affects them.

SPRYCEL contains lactose monohydrate

SPRYCEL contains lactose. Patients with rare hereditary conditions of lactose/fructose or galactose intolerance should not take SPRYCEL. Talk to your doctor before taking SPRYCEL if you are lactose intolerant.

3. How to take SPRYCEL

Do not share medicines prescribed for you with any other person.

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

The usual dose is:

- The recommended starting dose for SPRYCEL in patients with chronic phase CML is 100 mg once daily, with or without a meal. The recommended starting dose for SPRYCEL in patients with accelerated, myeloid or lymphoid blast phase CML or Ph+ ALL is 70 mg twice daily, with or without a meal. Try to take SPRYCEL at the same time each day.
- Swallow SPRYCEL tablets whole. Do not break, cut, chew or crush the tablets.
- Depending on your response to treatment and any side effects that you may experience, your doctor may adjust your dose of SPRYCEL upward or downward, or may temporarily discontinue SPRYCEL.

Your doctor will tell you how long your treatment with SPRYCEL will last. Do not stop treatment early. If you have the impression that the effect of SPRYCEL is too strong or too weak, tell you doctor or pharmacist.

If you take more SPRYCEL than you should

In the event of overdosage, consult your doctor or pharmacist. If neither is available, contact the nearest hospital or poison centre.

If you forget to take SPRYCEL

If you miss a dose of SPRYCEL, take your next scheduled dose at its regular time. Do not take a double dose to make up for forgotten individual doses. Call your doctor or pharmacist if you are not sure what to do.

4. Possible side effects

SPRYCEL can have side effects.

Not all side effects reported for SPRYCEL are included in this leaflet. Should your general health worsen or if you experience any untoward effects while taking **S**PRYCEL, please consult health care provider for advice.

The following information describes the most important side effects of SPRYCEL. It is not a comprehensive list of all side effects recorded in clinical trials with SPRYCEL. You should report any unusual symptoms to your doctor.

If any of the following happens, stop taking SPRYCEL and tell your doctor immediately or go to the casualty department at your nearest hospital:

- swelling of the hands, feet, ankles, face, lips and mouth or throat, which may cause difficulty in swallowing or breathing,
- rash or itching,
- fainting

These are all very serious side effects. If you have them, you may have had a serious reaction to SPRYCEL. You may need urgent medical attention or hospitalisation.

Tell your doctor immediately or go to the casualty department at your nearest hospital if you notice any of the following:

- 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

These are all serious side effects. You may need urgent medical attention.

Tell your doctor if you notice any of the following:

Frequent side effects:

- **Infections** (including bacterial, viral and fungal), pneumonia, herpes viral infection, upper respiratory infection, serious infection of the blood or tissues (including fatal outcome)
- **Heart and lungs**: shortness of breath, cough, palpitations, irregular heart beat, congestive heart failure, cardiac dysfunction, high blood pressure, increased blood pressure in the arteries that supply the lungs

- **Digestive problems**: diarrhoea, feeling or being sick (nausea, vomiting), 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 rash, fever, swelling around the face, hands and feet, headache, feeling tired or weak, bleeding, 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, haematoma, depression, insomnia, flushing, dizziness, contusion (bruising), anorexia, somnolence, generalised oedema
- **Pain**: pain in the muscles, abdominal (tummy) pain, pain in joints, muscular weakness, chest pain, pain around hands and feet, chills, stiffness in muscles and joints, muscle spasm
- **Tests may show**: low blood platelet count, low white blood cell count (neutropenia), anaemia, fluid around the lungs, fluid around the heart, fluid in the lungs, dysrhythmia, febrile neutropenia, gastrointestinal bleeding, high uric acid levels in the blood.

Less frequent side effects:

- **Heart and lungs**: heart attack (including fatal outcome), inflammation of the lining (fibrous sack) surrounding the heart, irregular heart rhythm, 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, 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**: 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), 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**: 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 characterised 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, 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
- **Pain**: inflammation of vein which can cause redness, tenderness and swelling, inflammation of the tendon
- **Brain:** loss of memory, stroke, temporary episode of neurologic dysfunction caused by loss of blood flow, facial nerve paralysis, dementia
- **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).

If you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

Your healthcare provider will monitor your blood counts frequently after you start SPRYCEL, and may adjust your dose of SPRYCEL or withhold SPRYCEL temporarily in the event your blood counts drop too low. In some cases, you may need to receive transfusions of red blood cells or platelets. Notify your doctor immediately if you develop a fever while taking SPRYCEL.

Reporting of side effects

If you get side effects, talk to your doctor, pharmacist or nurse. You can also report side effects to SAHPRA via the "**6.04 Adverse Drug Reaction Reporting Form**", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8. By reporting side effects, you can help provide more information on the safety of SPRYCEL.

5. How to store SPRYCEL

Store all medicines out of reach of children.

- Store at or below 30 ºC.
- SPRYCEL tablets do not require refrigeration.
- Keep the container well closed after first opening.
- Do not use after the expiry date stated on the label.
- Return all unused medicine to your pharmacist.
- Do not dispose of unused medicine in drains or sewerage systems (e.g. toilets).

6. Contents of the pack and other information

What SPRYCEL contains

The active substance is dasatinib

The other ingredients are:

Tablets:

croscarmellose sodium

hydroxypropyl cellulose

lactose monohydrate

magnesium stearate

microcrystalline cellulose

Film coating:

Opadry® white contains:

hypromellose 6 cP

polyethylene glycol 400

titanium dioxide

What SPRYCEL looks like and contents of the pack

SPRYCEL 20 mg tablets are available as white to off-white, round, biconvex, film-coated tablets with “BMS” debossed on one side and “527” on the other side.

SPRYCEL 50 mg tablets are available as white to off-white, oval, biconvex, film-coated tablets with “BMS” debossed on one side and “528” on the other side.

SPRYCEL 70 mg tablets are available as white to off-white, round, biconvex, film-coated tablets with “BMS” debossed on one side and “524” on the other side.

SPRYCEL 100 mg tablets are available as white to off-white, oval, biconvex, film-coated tablets with “BMS 100” debossed on one side and “852” on the other side.

SPRYCEL 20, 50, 70 mg film-coated tablets are packaged in white square, high density polyethylene (HDPE) bottles with white two-piece child-resistant, continuous thread (CRCT) closures having an aluminium foil induction seal (inner seal). Each bottle contains 60 tablets. The bottles will contain a cotton coiler and one silica gel desiccant canister.

SPRYCEL 100 mg film-coated tablets are packaged in white square, high density polyethylene (HDPE) bottles with white two-piece child-resistant, continuous thread (CRCT) closures having an aluminium foil induction seal (inner seal). Each bottle contains 30 tablets. The bottles will contain one silica gel desiccant canister.

Holder of Certificate of Registration

Equity Pharmaceuticals (Pty) Ltd*

100 Sovereign Drive

Route 21 Corporate Park

Nellmapius Drive

Irene, Pretoria

Tel no: 012 345 1747

This leaflet was last revised in

20 October 2022

Registration number

SPRYCEL 20 mg tablets: 41/26/1039

SPRYCEL 50 mg tablets: 41/26/1040

SPRYCEL 70 mg tablets: 41/26/1041

SPRYCEL 100 mg tablets: 44/26/0205

*SPRYCEL is a trademark of Bristol-Myers Squibb Holdings Ireland, used under license by Equity Pharmaceuticals (Pty) Ltd.