PART III: CONSUMER INFORMATION

PrSPRYCEL®
(dasatinib)

This leaflet is part III of a three-part "Product Monograph" published when SPRYCEL was approved for sale in Canada and is designed specifically for Consumers. This leaflet is a summary and will not tell you everything about SPRYCEL. Contact your doctor or pharmacist if you have any questions about the drug.

ABOUT THIS MEDICATION

What the medication is used for:

SPRYCEL (dasatinib) is used to treat adults who have:

- newly diagnosed Philadelphia chromosome positive (Ph+) chronic myeloid leukemia (CML) in chronic phase
- Ph+ CML who are no longer benefiting from other available therapies for CML, including imatinib mesylate (Gleevec®)
- a particular form of Ph+ acute lymphoblastic leukemia (ALL).

What it does:

Chronic myeloid leukemia or CML is one form of leukemia. In CML, myeloid white blood cells multiply in an uncontrolled manner. It may take years for CML to progress because it is a slow-growing or chronic cancer. There are three phases of CML: chronic phase, accelerated phase, and blast crisis phase. As CML progresses, patients advance through these phases.

Ph+ acute lymphoblastic leukemia or Ph+ ALL is another form of leukemia. Acute leukemias progress faster than chronic leukemias. In Ph+ ALL, lymphoblastic white blood cells multiply in an uncontrolled manner.

The active ingredient of SPRYCEL is dasatinib. Dasatinib acts by inhibiting the activity of proteins within the leukemia cells of patients with CML. These proteins are responsible for the uncontrolled growth of the leukemia cells.

When it should not be used:

- If you have a history of allergic reactions to dasatinib or to any other ingredients in SPRYCEL (See the "*What the important non-medicinal ingredients are*" section of this leaflet for a complete list of ingredients in SPRYCEL). Tell your healthcare provider if you think you have had an allergic reaction to any of these ingredients.
- Do not breast-feed if you are taking SPRYCEL.

SPRYCEL should not be used in children under two years of age.

What the medicinal ingredient is:
The active ingredient of SPRYCEL is dasatinib.

What the important non-medicinal ingredients are:
Croscarmellose sodium, hydroxypropyl cellulose, lactose monohydrate, magnesium stearate and microcrystalline cellulose. The tablet coating consists of hypromellose, titanium dioxide, and polyethylene glycol.

What dosage forms it comes in:

SPRYCEL (dasatinib) is available in film coated tablets for oral administration in strengths 20, 50, 70, 80, 100 and 140 mg dasatinib (as monohydrate).

WARNINGS AND PRECAUTIONS

Serious Warnings and Precautions:
SPRYCEL should be given under the supervision of a doctor experienced in the use of anti-cancer drugs. Serious and common side effects with SPRYCEL include:

- Myelosuppression (decrease of production of blood cells),
- Bleeding which may result in death,
- Fluid retention,
- Congestive heart failure (shortness of breath, swelling, weight gain) accompanied in most if not all cases by fluid retention and pulmonary edema (fluid in the lung),
- Pulmonary Arterial Hypertension (increase in blood pressure in the arteries supplying the lungs).

BEFORE you use SPRYCEL talk to your doctor or pharmacist if you:

- are pregnant or planning to become pregnant. SPRYCEL can harm the fetus when given to a pregnant woman. Women should not become pregnant while undergoing treatment with SPRYCEL.
- are breast-feeding. Do not breast-feed if you are taking SPRYCEL.
- are a sexually active male or female. Men and women who take SPRYCEL are advised to use highly effective contraception.
- have a liver problem.
- have a heart problem, such as arrhythmia, long QT syndrome (a hereditary disorder of the heart electrical rhythm).
- have ever had or might now have a hepatitis B infection (an infection of the liver). This is because SPRYCEL could cause the hepatitis B virus to become active again, which can be fatal in some cases. Your doctor will check for signs of this infection before treatment with SPRYCEL is started. If the hepatitis B virus is found,

you will be monitored closely during and for several months after treatment with SPRYCEL.
- are lactose intolerant or have been diagnosed with an intolerance to some sugars.
- are taking medicines to thin the blood or prevent clots. SPRYCEL may cause bleeding.

Talk to you doctor or pharmacist if you have:
- muscle aches/pains or weakness, or dark-colored urine.

INTERACTIONS WITH THIS MEDICATION

SPRYCEL may interact with other drugs, including those you take without a prescription. You must tell your doctor or pharmacist about all drugs, including prescription and non-prescription drugs, herbal products (e.g. St. John's Wort) and supplements you are taking or planning to take before you take SPRYCEL.

- Examples of medicines that increase the level of SPRYCEL in your bloodstream include ketoconazole, SPORANOX® (itraconazole), erythromycin, BIAXIN® (clarithromycin).
- Examples of medicines that decrease the amount of SPRYCEL in your bloodstream include dexamethasone, phenytoin, carbamazepine, rifampicin, and phenobarbital.
- Examples of a medicine whose blood levels might be altered by SPRYCEL include SANDIMMUNE®/NEORAL® (cyclosporine), simvastatin.

The absorption of SPRYCEL from your stomach into your bloodstream is best accomplished in the presence of stomach acid. You should avoid taking medicines that reduce stomach acid such as cimetidine, famotidine, ranitidine, or omeprazole while taking SPRYCEL. Medicines that neutralize stomach acid, such as aluminium hydroxide/magnesium hydroxide, calcium carbonate or calcium carbonate and magnesia may be taken up to 2 hours before or 2 hours after SPRYCEL.

Since SPRYCEL therapy may be associated with bleeding events, tell your doctor if you are regularly using blood thinners, including medications such as warfarin sodium or aspirin.

PROPER USE OF THIS MEDICATION

Usual dose:

The usual dose for chronic phase CML is 100 mg once a day, either in the morning or in the evening.

The usual dose for accelerated or blast crisis CML or Ph+ALL is 140 mg once daily, either in the morning or in the evening.

The tablets should be swallowed whole, not crushed. They can be taken with or without food. Try to take SPRYCEL at the same time each day.

Avoid taking grape fruit juice since it may increase the blood levels of SPRYCEL.

Overdose:

In case of drug overdosage, contact a healthcare practitioner (e.g. doctor) hospital emergency department or regional poison control centre, even if there are no symptoms.

Missed Dose:

If you miss a dose of SPRYCEL, take your next scheduled dose at its regular time. Do not take two doses at the same time. Call your healthcare provider or pharmacist if you are not sure what to do.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

Most patients taking SPRYCEL will experience some mild to moderate side effects. Most side effects can be managed by your doctor through additional medications, dose adjustments, or other measures.

The following information describes the most important side effects of which you must be aware. 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.

Common side effects of SPRYCEL therapy include diarrhea, fever, headache, fatigue, nausea, skin rash, shortness of breath, cough, vomiting, pain, stomach pain, infection, upper respiratory tract infection, muscle aches, joint aches, and bone and extremity pain.

Other important common side effects include**:**

- **Low Blood Counts**: As with many leukemia drugs, therapy with SPRYCEL can be associated with low red blood cell counts (anemia), low white blood cell counts (neutropenia), and low platelet counts (thrombocytopenia). Your doctor will monitor your blood counts frequently after you start SPRYCEL, and may adjust your dose of SPRYCEL or withhold the drug temporarily in the event your blood counts drop too low, or administer additional supportive medicines to help your body regain normal blood levels. In the most severe cases, you may need to receive transfusions of red blood cells or platelets. If you develop a fever while your blood counts are depressed, you should notify your doctor immediately.

- **Bleeding:** Therapy with SPRYCEL may be associated with bleeding from a variety of sources. The most serious bleeding events observed in clinical studies

included bleeding from the gastrointestinal tract and, bleeding into the brain. Bleeding into the brain resulted in the death of nine patients (less than 1% of all patients in clinical trials). The serious bleeding events were associated with very low platelet counts. Less severe bleeding events included bleeding from the nose, the gums, bruising of the skin and excessive menstrual bleeding. Your doctor will monitor your blood counts regularly, but you should notify your physician immediately should you experience bleeding or easy bruising, no matter how mild.

- **Fluid Retention**: Therapy with SPRYCEL may be associated with fluid building up under the skin of your lower extremities and around your eyes. In more severe cases, fluid may accumulate in the lining of your lungs, the sac around your heart, or your abdominal cavity. If you experience swelling, weight gain, or increasing shortness of breath it could be the result of fluid retention and you should report these events immediately to your doctor. Your doctor can manage fluid retention in a variety of ways while you are receiving SPRYCEL.

- **Heart Rhythm Change**: SPRYCEL has the potential to induce changes in heart rhythm in susceptible individuals who have certain inherited cardiac syndromes, take medication to control heart rhythm, or are prone to low levels of potassium or magnesium in their blood. Your doctor can assess your risk by reviewing the complete list of medications that you are taking and by monitoring the potassium and magnesium levels in your blood and electrocardiogram.

Other important uncommon side effects include:

- **Liver toxicity**: Liver problems such as liver inflammation and increased liver enzyme levels.

Other important rare side effects include:

- **Pulmonary Arterial Hypertension** (increase in blood pressure in the arteries supplying the lungs): SPRYCEL has been associated with an increase in blood pressure in the arteries supplying the lungs. Your doctor will assess your lung and heart function before and during the treatment of SPRYCEL.

- **Severe Reaction Involving Skin and Other Organs:** A serious skin reaction known as Stevens-Johnson syndrome has been reported with SPRYCEL. Very rarely, severe forms of this reaction may lead to death. Serious cases of another skin reaction known as erythema multiforme have also been reported with SPRYCEL. Stop taking the drug and seek immediate medical attention if you develop any combination of fever, sore mouth or throat, and blistering and/or peeling of your skin or mucous membranes (Stevens-Johnson syndrome) or raised red or purple skin patches with itching, burning pustular eruption (erythema multiforme).

Based on ongoing monitoring after the approval of SPRYCEL, the following events have been reported: inflammation of the lungs, blood clots in the blood vessels, irregular heart rhythm, and deaths from gastrointestinal bleeding. These events may or may not have been related to SPRYCEL.

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM

Symptom / effect		Talk with your doctor or pharmacist		Stop taking drug and call your doctor or pharmacist
		Only if severe	In all cases	
Common	Bleeding or bruising without having an injury no matter how mild, blood in vomit, stools or urine, or black stools		√	
Common	Fever, severe chills (these can be signs of infections)		√	
Common	Swelling, weight gain, increasing shortness of breath, especially if this occurs after low levels of physical exertion; chest pain when taking a deep breath (these could be signs of fluid retention)		√	
Common	Dizziness and/or feeling faint		√	
Common	Irregular and/or forceful heart beat			√
Uncommon	Symptoms of muscle aches/pains or weakness, or dark urine		√	

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM

Symptom / effect		Talk with your doctor or pharmacist		Stop taking drug and call your doctor or pharmacist
		Only if severe	In all cases	
Uncommon	Yellow skin and eyes, nausea, loss of appetite, dark-coloured urine (liver damage)		√	
Rare	Shortness of breath and fatigue (these could be signs of increased blood pressure in the arteries supplying the lungs)		√	
Reported from post-marketing with unknown frequency	Weight loss, fever, abdominal pain, nausea and vomiting followed by jaundice (yellowing of the skin or whites of eyes) (these could be signs of a hepatitis B infection becoming active again when you have had hepatitis B in the past)		√	
Reported from post-marketing with unknown frequency	Severe skin reaction with fever, sore mouth or throat, blistering and/or peeling of your skin or mucous membranes. "Stevens-Johnson syndrome" or raised red or purple skin patches with itching, burning pustular eruption "erythema multiforme"			√

This is not a complete list of side effects. For any unexpected effects while taking SPRYCEL, contact your doctor or pharmacist.

HOW TO STORE IT

SPRYCEL (dasatinib) tablets should be stored at room temperature between 15°C to 30° C. Keep out of the reach and sight of children.

Do not use SPRYCEL after the expiry date which is stated on the label after EXP.

REPORTING SUSPECTED SIDE EFFECTS

To monitor drug safety, Health Canada through the Canada Vigilance Program collects information on serious and unexpected side effects of drugs. If you suspect you have had a serious or unexpected reaction to this drug you may notify Canada Vigilance:

By toll-free telephone: 866-234-2345
By toll-free fax: 866-678-6789
Online: www.healthcanada.gc.ca/medeffect
By email: CanadaVigilance@hc-sc.gc.ca

By regular mail:
Canada Vigilance National Office
Marketed Health Products Safety
and Effectiveness Information Bureau
Marketed Health Products Directorate
Health Products and Food Branch
Health Canada
Tunney's Pasture, AL 0701C
Ottawa ON K1A 0K9

NOTE: Should you require information related to the management of the side effect, please contact your health care provider before notifying Canada Vigilance. The Canada Vigilance Program does not provide medical advice.

MORE INFORMATION

This document plus the full product monograph, prepared for health professionals can be obtained by contacting the sponsor, Bristol-Myers Squibb Canada, at 1-866-463-6267.

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