

17.7 Fatigue

Patients should be informed that they may experience fatigue with SPRYCEL. If this symptom is significant, they should seek medical attention.

17.8 Rash

Patients should be informed that they may experience skin rash with SPRYCEL. If this symptom is significant, they should seek medical attention.

17.9 Lactose

Patients should be informed that SPRYCEL contains 135 mg of lactose monohydrate in a 100-mg daily dose and 189 mg of lactose monohydrate in a 140-mg daily dose.

Manufactured by:

Bristol-Myers Squibb Company

Princeton, NJ 08543 USA

US Patent No 6,596,746

Bristol-Myers Squibb Company

Princeton, NJ 08543 USA

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17.10 FDA-Approved Patient Labeling

SPRYCEL[®] (dasatinib) Tablets

What is SPRYCEL?

SPRYCEL (dasatinib) is a prescription medicine used to treat adults who have chronic myeloid leukemia (CML) and to treat adults who have a particular form of acute lymphoblastic leukemia (ALL) called Philadelphia chromosome positive or Ph⁺ ALL. It is intended for use in patients who are no longer benefiting from treatment with the current available therapies for these diseases (resistance), including a medicine called

GLEEVEC[®] (imatinib mesylate). It may also be used in patients who experience severe side effects from GLEEVEC and are no longer able to take it (intolerance). The long-term benefits and toxicities of SPRYCEL are currently still being studied. SPRYCEL has not been studied in children.

What is Leukemia?

Leukemia is a cancer of white blood cells, which grow in the bone marrow. In leukemia, white blood cells multiply in an uncontrolled manner, occupying the bone marrow space and spilling out into the bloodstream. As a consequence, the production of normal red blood cells (oxygen carrying cells), white blood cells (cells which fight infection), and platelets (cells which help blood clot) is compromised. Therefore, patients with leukemia are at risk of serious anemia, infections, and bleeding.

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. As CML progresses, patients advance through three phases: chronic phase, accelerated phase, and blast crisis phase. 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.

How does SPRYCEL work?

The active ingredient of SPRYCEL is dasatinib. Dasatinib reduces the activity of one or more proteins responsible for the uncontrolled growth of the leukemia cells of patients with CML or Ph+ ALL. This reduction allows the bone marrow to resume production of normal red cells, white cells, and platelets.

Who should not take SPRYCEL?

- SPRYCEL is currently not recommended for patients who have not previously had a trial of GLEEVEC[®] (imatinib mesylate).
- Women who are pregnant or planning to become pregnant should not take SPRYCEL (see below).

What should I tell my healthcare provider before I take SPRYCEL?

Tell your healthcare provider about all of your medical conditions, including if you:

- **are pregnant or planning to become pregnant.** SPRYCEL may harm the fetus when given to a pregnant woman. Women should avoid becoming pregnant while undergoing treatment with SPRYCEL. Tell your healthcare provider *immediately* if you become pregnant or plan to become pregnant while taking SPRYCEL.
- **are breast-feeding.** It is not known if SPRYCEL can pass into your breast milk or if it can harm your baby. Do not breast-feed if you are taking SPRYCEL.
- **are a sexually active male.** Men who take SPRYCEL are advised to use a condom to avoid pregnancy in their partner.
- have a liver or heart problem.
- are lactose intolerant.

Can I take other medicines with SPRYCEL?

Tell your healthcare provider about all the medicines you take including prescription and over-the-counter medicines, vitamins, antacids, and herbal supplements.

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 NIZORAL[®] (ketoconazole), SPORANOX[®] (itraconazole), NORVIR[®] (ritonavir), REYATAZ[®] (atazanavir sulfate), CRIXIVAN[®] (indinavir), VIRACEPT[®] (nelfinavir), INVIRASE[®] (saquinavir), KETEK[®] (telithromycin), E-MYCIN[®] (erythromycin), and BIAXIN[®] (clarithromycin).
- Medicines that decrease the amount of SPRYCEL in your bloodstream are DECADRON[®] (dexamethasone), DILANTIN[®] (phenytoin), TEGRETOL[®] (carbamazepine), RIMACTANE[®] (rifampin), and LUMINAL[®] (phenobarbital).

- Medicines whose blood levels might be altered by SPRYCEL are SANDIMMUNE[®] (cyclosporine), ALFENTA[®] (alfentanil), FENTANYL[®] (fentanyl), ORAP[®] (pimozide), RAPAMUNE[®] (sirolimus), PROGRAF[®] (tacrolimus), and ERGOMAR[®] (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 TAGAMET[®] (cimetidine), PEPCID[®] (famotidine), ZANTAC[®] (ranitidine), PRILOSEC[®] (omeprazole), PROTONIX[®] (pantoprazole sodium), NEXIUM[®] (esomeprazole), ACIPHEX[®] (rabeprazole), or PREVACID[®] (lansoprazole) while taking SPRYCEL. Medicines that neutralize stomach acid, such as MAALOX[®] (aluminum hydroxide/magnesium hydroxide), TUMS[®] (calcium carbonate), or ROLAIDS[®] (calcium carbonate and magnesia) 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 COUMADIN[®] (warfarin sodium) or aspirin.

How should I take SPRYCEL?

- If you have chronic phase CML, the usual dose is 100 mg (two 50-mg tablets) once daily, either in the morning or in the evening.
- If you have accelerated or blast crisis CML or Ph+ ALL, the usual dose is 70 mg (one 70-mg tablet) twice daily, once in the morning and once in the evening.
- SPRYCEL can be taken with or without a meal. Try to take SPRYCEL at the same time each day.
- Take SPRYCEL whole. Do not break, cut, or crush the tablets.
- Do not drink grapefruit juice while taking SPRYCEL.
- **Depending on your response to treatment and any side effects that you may experience, your healthcare provider may adjust your dose of SPRYCEL upward or downward, or may temporarily discontinue SPRYCEL.**
- **You should not change your dose or stop taking SPRYCEL without first talking with your healthcare provider.**

- **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.
- **If you accidentally take more than the prescribed dose of SPRYCEL**, call your healthcare provider right away.

What are the possible side effects of SPRYCEL?

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 healthcare provider.

- **Low Blood Counts:** SPRYCEL may cause low red blood cell counts (anemia), low white blood cell counts (neutropenia), and low platelet counts (thrombocytopenia). Your healthcare provider 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. In some cases, you may need to receive transfusions of red blood cells or platelets. **Notify your healthcare provider immediately if you develop a fever while taking SPRYCEL.**
- **Bleeding:** SPRYCEL may cause bleeding. The most serious bleeding events observed in clinical studies included bleeding into the brain leading to death in <1% of patients, and bleeding from the gastrointestinal tract. Less severe events included bleeding from the nose, the gums, bruising of the skin, and excessive menstrual bleeding. **Notify your healthcare provider immediately if you experience bleeding or easy bruising while taking SPRYCEL.**
- **Fluid Retention:** SPRYCEL may cause fluid to accumulate in your legs 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. **Notify your healthcare provider immediately if you experience swelling, weight gain, or increasing shortness of breath while taking SPRYCEL.**

Other common side effects of SPRYCEL therapy include diarrhea, headache, skin rash, nausea, fatigue, and shortness of breath.

In clinical trials of 2182 patients, 10% (10 out of 100) of patients permanently stopped SPRYCEL therapy because of side effects.

How will I know if SPRYCEL is working?

How well you respond to SPRYCEL therapy may depend on several factors, including the phase of your disease, prior treatments, or other factors your healthcare provider may discuss with you. General treatment goals for patients treated with SPRYCEL include a reduction in the number of leukemia cells and improvement or normalization of the white blood cell, red blood cell, and platelet counts.

While you are on SPRYCEL, your healthcare provider will monitor these responses through routine blood tests. The type and frequency of these tests will be determined by your healthcare provider and may vary depending on the status of your disease.

How should I store SPRYCEL?

- Store SPRYCEL (dasatinib) Tablets at room temperature, 59° to 86° F (15° to 30° C). SPRYCEL Tablets do not require refrigeration.
- Keep the container tightly closed.
- Throw away SPRYCEL when it is outdated. Ask your pharmacist how to properly dispose of SPRYCEL.
- **Keep SPRYCEL and all medicines out of the reach of children and pets.**

General information about SPRYCEL: This medicine was prescribed for your particular condition and should be used only by you under the close supervision of your healthcare provider. The leaflet summarizes the most important information about SPRYCEL. If you would like more information, talk with your healthcare provider. If you have questions or concerns, or want more information about SPRYCEL, your healthcare provider and pharmacist have the complete prescribing information upon which this guide is based. You may want to read it and discuss it with your healthcare provider. Remember, no written summary can replace careful discussion with your healthcare provider.

What are the ingredients in SPRYCEL?

Active Ingredient: dasatinib

Inactive Ingredients: lactose monohydrate, microcrystalline cellulose, croscarmellose sodium, hydroxypropyl cellulose, and magnesium stearate. The tablet coating consists of hypromellose, titanium dioxide, and polyethylene glycol.

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