

Dasatinib (for chronic myeloid leukemia)

Product:

DASATINIB (Sprycel®)
20mg, 50mg, 70mg tablets

Class of drugs:

Multi-kinase inhibitor

Indication:

Treatment of chronic myeloid leukemia

Manufacturer:

Bristol-Myers Squibb Canada

CED Recommendation

The CED recommended dasatinib (Sprycel) be funded through the Exceptional Access Program for adult patients with chronic myeloid leukemia according to specific criteria. The CED's recommendation was made on the basis that evidence supports the use of dasatinib (Sprycel) in patients who do not respond to, or are intolerant of standard treatment.

Executive Officer Decision

Based on the CED's recommendation, the Executive Officer decided to fund dasatinib (Sprycel) through the Exceptional Access Program for chronic myeloid leukemia according to specific criteria.

Status

Funding available through the Ontario Public Drug Programs via the Exceptional Access Program.

Highlights of Recommendation:

- ◆ Dasatinib (Sprycel) is an oral drug used to treat chronic myeloid leukemia (CML) in adults who do not respond to, or cannot tolerate the side effects of imatinib, the current standard treatment for CML.
- ◆ The Committee reviewed one study in which CML patients whose disease had not responded to imatinib at regular doses were given either dasatinib (Sprycel) or high-dose imatinib. The study found that dasatinib (Sprycel) was more effective than high-dose imatinib in patients whose disease had not responded to regular-dose imatinib.
- ◆ Side effects with dasatinib (Sprycel) include low blood cell count, diarrhea, nausea, water retention (e.g., swollen ankles), pleural effusion (fluid collecting around the lungs), skin rash, and muscle or joint pain.
- ◆ The cost of dasatinib (Sprycel) ranges from \$137 to \$151 per day (based on a daily dose of 100mg to 140mg). This is less expensive than high-dose imatinib (800mg daily) at \$205 per day.
- ◆ **Overall, the Committee agreed that dasatinib (Sprycel) provides a treatment option for CML patients who do not respond or are intolerant to imatinib.**

Background:

Chronic myeloid leukemia (CML) is a type of blood cancer. The disease is linked to an abnormal chromosome, called the Philadelphia chromosome, in the blood-forming cells of the bone marrow. The Philadelphia chromosome leads to an overproduction of immature, poorly functioning white blood cells.

There are three phases to this disease: the chronic phase, in which the disease is stable; the accelerated phase, in which the disease has become more aggressive; and the blast phase, in which the disease has become terminal.

The standard treatment for CML is a drug called imatinib. Imatinib is a targeted therapy, and it acts on the abnormal protein produced by the Philadelphia chromosome. Imatinib is listed on the Ontario Drug Benefit Formulary for the treatment of CML.

Some patients do not respond to imatinib, and some may initially respond then become resistant to treatment. Additionally, some patients experience intolerable side effects on this drug. Prior to the availability of other targeted drugs like dasatinib (Sprycel), bone marrow transplantation was the only treatment option for patients whose disease was imatinib-resistant or who could not tolerate imatinib. Dasatinib (Sprycel) works against the same abnormal protein targeted by imatinib, but in slightly different ways.

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Detailed Discussion:

- ◆ The Committee reviewed dasatinib (Sprycel) for the treatment of CML on two occasions, initially in August 2007 and again in June 2008.
 - ◆ The focus of the review was a randomized controlled trial (*Kantarjian et al. Blood 2007;109(12):5143-50*) that compared dasatinib (Sprycel) to high-dose (800mg) imatinib in patients with chronic phase CML who did not respond to 400mg or 600mg doses of imatinib. The study reported that the rate of cytogenetic response (a positive response to treatment), defined by a reduction in the number of cells with the abnormal Philadelphia chromosome, was significantly higher in patients on dasatinib (Sprycel) compared with patients on high-dose imatinib.
 - ◆ In terms of side effects, the study found that, compared with imatinib, dasatinib (Sprycel) is associated with a higher incidence of neutropenia (low white blood cell count), thrombocytopenia (low platelet count), pleural effusion (fluid collecting around the lungs), fatigue and headache; imatinib is associated with more water retention and stomach disturbance.
 - ◆ There are currently no randomized controlled trials comparing dasatinib (Sprycel) to imatinib in the accelerated or blast phase of the disease.
 - ◆ The cost of dasatinib (Sprycel) ranges from \$137 to \$151 per day (based on a daily dose of 100mg to 140mg). This is less expensive than high-dose imatinib (800mg daily) at \$205 per day. For patients with chronic phase CML who are resistant or intolerant to imatinib, dasatinib (Sprycel) has been demonstrated to be a cost-effective treatment option. In the accelerated and blast phases of the disease, the cost-effectiveness of dasatinib is less certain, because its relative efficacy compared with imatinib has not been assessed.
- ◆ Overall, the Committee noted that there are no treatment alternatives for CML patients whose disease is resistant to imatinib, other than a bone marrow transplant. The Committee indicated that dasatinib (Sprycel) provides a treatment option for patients with chronic phase CML who are resistant or intolerant to imatinib and for patients who have progressed to accelerated phase or blast crisis while on imatinib.
 - ◆ The Committee recommended that dasatinib (Sprycel) be funded through the Exceptional Access Program (EAP) according to the following criteria:
 - *For adult patients with chronic phase CML with primary or acquired resistance to imatinib 600mg per day. Dosing recommendation: 100mg per day or 70mg two times daily.*
 - *For adult patients with chronic phase CML who progress to accelerated phase on imatinib 600mg per day. Dosing recommendation: 140mg per day.*
 - *For adult patients with chronic phase CML who have blast crisis while on imatinib 600mg per day. Dosing recommendations: 140mg per day.*
 - *For adult patients with CML who cannot tolerate imatinib or have experienced Grade 3 or higher toxicities to imatinib.*
 - ◆ The CED worked jointly with a subcommittee involving cancer experts to review this cancer drug, as is done for all other cancer drug treatments.

Cancer Care Ontario (CCO) Information:

Information on CCO chemotherapy regimens for CML can be found at:

http://www.cancercare.on.ca/index_chemoRegimensbyDisease.htm

The Hematology Disease Site Group Program in Evidence-Based Care Guideline for dasatinib (Sprycel) in CML is available at:

<http://www.cancercare.on.ca/english/home/toolbox/qualityguidelines/other-reports/evaldrug-rep/>



Ministry of
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