

Record of Recommendation

Re: Funding Dasatinib (Sprycel®) in CML and Ph+ALL

January 9, 2008

Discussion facilitated using the Decision Making Framework.

- All present will vote electronically when the vote is called by the chair. The voting process will be completed by 5 pm on January 24th. The decision will be made by a majority with dissenting voters given the opportunity to record their opinion. Dissenting opinions must be recorded within seven days of the result of the vote being announced.
- Core values and principles were reviewed and discussed along with competing obligations, constraints and relevant information.
- Options for a recommendation to the Deputy Minister were reviewed and each option was discussed. Two options were identified at this time:
 - 1) Approval of funding with restrictions
 - 2) Denial of funding
- An analysis of the projected benefits and burdens of each option was discussed.

Projected Benefits: as second line therapy in the treatment of chronic myeloid leukemia (CML) and acute lymphoblastic leukemia (ALL).

- ✓ Chronic Myeloid Leukemia (CML) is a malignant clonal disorder of hematopoietic stem cells in the bone marrow characterized by increased WBC
- ✓ Acute Lymphoblastic Leukemia (ALL) is a clonal expansion of lymphoid blasts in bone marrow, blood, and other tissue.
- ✓ The standard of care in CML is imatinib (Gleevec®), an oral inhibitor of BCR-ABL tyrosine kinase, as 1st line treatment.
- ✓ 2nd line treatment is an allogeneic stem cell transplant but only if a donor is available and age<55. There aren't any good treatment options available for 2nd-

line therapy if the patient is not eligible for allogeneic stem cell transplant (the majority of patients).

- ✓ In ALL the standard therapy is imatinib (Gleevec[®]) + chemotherapy as first line. This has improved overall survival to 60-70% at 1 year. Allogeneic stem cell transplant is used as adjunctive therapy if donor available and age<55. The use of imatinib (Gleevec[®]) has improved the ability of patients to receive allogeneic stem cell transplant. There have been few treatment options available for 2nd-line therapy until now.
- ✓ The clinical trials for dasatinib (Sprycel[®]) are Phase II trials of imatinib-resistant or intolerant patients with chronic phase, accelerated phase and blast crisis CML and Ph+ ALL.
- ✓ Complete hemotologic response (CHR) was 90% in chronic phase CML, 33% in accelerated phase CML, 26% in Blast Phase CML and 33% in Ph+ ALL.
- ✓ Major cytogenetic response (MCyR) was 52% in chronic phase CML, 32% in accelerated phase CML and 30-50% in Blast Phase CML.
- ✓ Complete cytogenetic response (CCyR) was 33% in Ph+ ALL.
- ✓ Progression free survival (PFS) was 90% at 12 months in chronic phase CML, 66% at 12 months in accelerated phase CML, 3-6.7 months in Blast Phase CML and 3.7 months in Ph+ ALL.
- ✓ There is also a randomized phase II trial of imatinib (Gleevec[®]) vs dasatinib (Sprycel[®]) that showed a better response with dasatinib:
 - CHR 93% vs 82%
 - MCyR 52% vs 33%
 - PFS 93% vs 54%
- ✓ Discontinuation of therapy was more common in the 800 mg imatinib (Gleevec[®]) arm 18% vs 7% due to toxicity, 55% vs 8% due to lack of response or progression

Projected Burdens:

- ✓ The drug cost only per patient is approx. \$137.00 - \$151.00 per day depending on dose.
- ✓ For patients in chronic phase CML, dasatinib is cost saving, since it is more effective and less costly with an estimated cost per quality adjusted life year of approx. \$ -142,601.
- ✓ For patients in the accelerated phase, dasatinib presents an \$88,098 increase in cost per QALY gained.
- ✓ For patients in the blast phase, dasatinib presents a \$173,922 increase in cost per QALY gained.
- ✓ There is no estimate for cost per quality adjusted life year in Ph+ ALL.
- ✓ The budget impact is difficult to predict as it could result in an incremental increase of approx \$ 25,000 in the remainder of 2007/08, \$423,000 (8 patients) in 2008/09 and \$528,000 (10 patients) in 2009/10 if patients were not treated with imatinib. However it could also result in cost savings by avoiding the increase in imatinib dose to 800 mg/day which would be \$15,000 per patient more expensive per year.

The vote was conducted electronically. The question the Committee was asked to vote on is:

“Should the Committee support a recommendation to the Deputy Minister of Health to publicly fund dasatanib (Sprycel[®]) as a single agent for the treatment of adults with chronic, accelerated or blast phase CML and Ph⁺ ALL with resistance or intolerance to prior therapy including imatinib (Gleevec[®]). These criteria include:

1. Patients with CML in chronic phase who are intolerant of imatinib.
 2. Patients with CML in chronic phase who are resistant (imatinib 600mg/day).
 3. Patients with CML that have progressed to accelerated phase or blast phase crisis while on therapy including imatinib.
 4. Patients with resistant or intolerant Ph⁺ ALL.
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- **The result of the vote was a majority in favor of recommending funding. There were no dissenting opinions recorded.**