

Record of Recommendation

Re: Funding Nilotinib (Tasigna[®]) for the treatment of Chronic Myeloid Leukemia (CML)

January 12, 2011

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 24, 2011. 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.

Background:

- ✓ CML is a malignant clonal disorder of hematopoietic stem cells. The median age of diagnosis is 53 years. Each year 10-15% of cases will transform from chronic phase to blast crisis. Without current treatments, the median survival is 20 months from diagnosis.
- ✓ Current standards of care in CML are imatinib (Gleevec[®]) which is used first line and dasatinib (Sprycel[®]) which is used as a second line therapy. Both agents are oral inhibitors of BCR-ABL tyrosine kinase.
- ✓ In the Pharmacare Programs, imatinib (Gleevec[®]) is insured as a first line therapy for CML and dasatinib (Sprycel[®]) is insured as a second line option.
- ✓ Nilotinib (Tasigna[®]) is also a BCR-ABL tyrosine kinase inhibitor. It has been studied in phase II studies in both chronic phase (CP) and accelerated phase (AP) CML.

Projected Benefits:

- ✓ In CML CP in patients with imatinib resistance or intolerance, overall major cytogenetic response (MCR) was 48% at 6 months and 59% at 24 months; complete hematological response (CHR) was 74% at 6 months and 95% at 24 months. Estimated 12 month overall survival was 95% and 24 month survival was 87%. This was a phase II open label trial with a single arm of treatment.
- ✓ In CML AP in patients with imatinib resistance or intolerance, CHR was 26% at 6 months and 31% at 11 months; MCR was 29% at 6 months and 32% at 11 months. Percentage of patients returning to chronic phase was 12% and 13% at 6 months and 11 months respectively. This was also a single arm, open label Phase 2 trial.
- ✓ Nilotinib has a side effect profile and resistance pattern which is different than dasatinib; having both available may allow more appropriate selection of therapy based on patient specific factors.

Projected Burdens:

- ✓ The most common adverse events were rash, nausea, pruritis, headaches, fatigue, constipation, diarrhea, and muscle spasm. Grade III or IV hematological abnormalities include neutropenia (21%-29%) and thrombocytopenia (29%- 35%). Elevations in AST, ALT, bilirubin, and lipase, and pancreatitis have been reported. Nilotinib may prolong the QT interval.
- ✓ The committee noted the lack of phase III studies and that therapy has been issued a conditional notice of compliance, pending confirmation of clinical benefit.

Result of Vote:

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

“Should the Committee support a recommendation to the Deputy Minister of Health to fund nilotinib as a single line agent for the treatment of adults with chronic or accelerated phase CML with resistance or intolerance to prior therapy. This would include

1. Patients with CML in chronic phase who are intolerant to imatinib or dasatinib or both.
 2. Patients with CML in chronic phase who are resistant to imatinib 600mg/day
 3. Patients with CML that have progressed to accelerated phase while on imatinib
- Sequential use of dasatinib and nilotinib is not permitted except in the circumstance described above (i.e. intolerance).

- The result of the vote was a majority recommending funding.
- This recommendation has been accepted by the Deputy Minister of Health and funding has been approved within the Nova Scotia Pharmacare Programs.