

Record of Recommendation

Re: Funding lenalidomide (Revlimid[®]) in Multiple Myeloma

March 10, 2010

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 March 19, 2010. 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:

- ✓ Multiple myeloma (MM) is a hematological malignancy of the plasma cells.
- ✓ There is no cure for MM however new approaches and use of multiple lines of therapy have changed the course of the disease with many patients living years after diagnosis.
- ✓ Possible therapies include analogous stem cell transplant (ASCT), melphalan plus prednisone, dexamethasone, cyclophosphamide plus prednisone, thalidomide with or without steroids and bortezomib.
- ✓ Lenalidomide (Revlimid[®]) is a new therapy for MM that is related to the drug thalidomide. Lenalidomide was previously reviewed by the CSTPC for the treatment of MM (January 2009) and funding was not recommended.

Projected Benefits:

- ✓ Two phase III studies (MM009 and 010) form the basis of the review of lenalidomide. These two studies compare lenalidomide/dexamethasone therapy to placebo/dexamethasone therapy.
- ✓ These studies demonstrate that lenalidomide/dexamethasone is superior to

placebo/dexamethasone therapy in important parameters including median time to progression (11.1 versus 4.7 months and 11.3 versus 4.7 months) and overall survival (29.6 versus 20.2 months and not reached versus 20.6 months).

- ✓ A subsequent pooled analysis (intention to treat) of these two studies showed a median survival of 35 months in the lenalidomide/dexamethasone group versus 31 months in the placebo/dexamethasone group, a four month difference.
- ✓ Interpretation of effects on overall survival is complicated by the fact that approximately 47% of patients in the placebo group had “crossed-over” to receive active treatment with lenalidomide upon treatment failure. This cross-over from placebo to active therapy can obscure the true difference in the two groups, likely over-estimating the benefit seen in the placebo/dexamethasone group.
- ✓ As comparison, data from trials using dexamethasone (UK Medical Research Council) suggest a survival with dexamethasone of 19.5 months for patients having used one prior therapy and 11.6 months for patients who had used more than one prior therapy.
- ✓ With the exception of dexamethasone, the benefits of lenalidomide versus other standard therapies in the treatment of MM is unknown.

Projected Burdens:

- ✓ The most frequently reported adverse events include neutropenia, muscle cramps, constipation, diarrhea, nausea, tremor, dizziness, fatigue, insomnia and infection.
- ✓ The estimated budget impact is approximately \$800,000 to \$1,000,000 per year for 10 to 12 patients.
- ✓ Applicable copayments and deductibles will apply to Pharmacare beneficiaries.
- ✓ Dispensing is limited to selected pharmacies and patients must enroll in a controlled access program.

Result of Vote:

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 fund lenalidomide in combination with dexamethasone in adult patients with progressive MM after at least one previous treatment, not resistant to dexamethasone, documented measurable disease and an ECOG performance status of 0 – 2.”

- **The result of the vote was a majority in favor of recommending funding.**
- **The Deputy Minister and Minister of Health have accepted this recommendation. Funding within the Nova Scotia Pharmacare Programs will begin March 1, 2011.**