

## **Record of Recommendation**

### **Re: Funding Rituximab (Rituxan<sup>®</sup>) for the treatment of Chronic Lymphocytic Leukemia**

**June 30, 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 July 12, 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:**

- ✓ Chronic lymphocytic leukemia (CLL) is the most common adult leukemia. The median age of diagnosis is 65-72 years and the average life expectancy is 7-10 years.
- ✓ CLL is incurable but is responsive to chemotherapy such as chlorambucil, fludarabine, and cyclophosphamide. These therapies induce remission but have no effect on overall survival. Fludarabine plus cyclophosphamide has demonstrated improvement in progression-free survival.
- ✓ Rituximab is a monoclonal antibody which targets CD20 positive lymphoma/leukemia cells.
- ✓ Two large trials have compared fludarabine, cyclophosphamide and rituximab (FCR) versus fludarabine and cyclophosphamide (FC).

### Projected Benefits:

- ✓ In previously untreated patients, FCR was superior to FC in terms of control rate (44.1% versus 21.8%), median progression free survival (51.8 months versus 32.8 months), and overall survival rate (87.2% versus 82.5%). Median overall survival was not reached in both arms (follow up 37.7 months). The trial was stopped prematurely based on positive results on progression free survival.
- ✓ In patients previously treated with one line of therapy, FCR was superior to FC in terms of control rate (24.3% versus 13%), median duration of response (39.6 months versus 27.2 months) and median progression free survival (30.6 months versus 20.6 months). Median overall survival was not significantly different (median follow-up 25 months). There are no clinical trials assessing re-treatment in patients who had previously responded well to rituximab.

### Projected Burdens:

- ✓ Toxicities include allergic infusion reactions, immunosuppression (minimal) and reactivation of viral infections. Similar toxicities were reported in the FC and FRC arms of the trial.
- ✓ The approximate cost per patient per 6 cycles is \$22,745. The estimated cost for 15 patients is \$342,000 per year.
- ✓ As a first line therapy versus FC, the estimated cost per life year gained (LYG) is \$24,526 and cost per quality adjusted life year (QALY) is \$28,315. As a second line therapy, the estimated cost per LYG is \$41,490 and the cost per QALY is \$49,199.

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### Result of Votes:

Two separate votes were conducted electronically. The questions the Committee was asked to vote on were:

“Should the Committee support a recommendation to the Deputy Minister of Health to fund rituximab (R) in combination with fludarabine and cyclophosphamide (FC) in previously untreated symptomatic patients with documented evidence of CD20- positive chronic lymphocytic leukemia (CLL) with an ECOG performance status of 0-2 and who choose to receive combination chemotherapy. FCR would be a reasonable option for CLL patients (including SLL) previously treated with chemotherapy but not exposed to a rituximab based regimen.”

- **The result of the vote was a majority in favor of recommending funding.**

“Should the Committee support a recommendation to the Deputy Minister of Health to fund rituximab (R) in combination with fludarabine and cyclophosphamide (FC) as an option in CLL patients (including SLL) with relapsed disease who have achieved a response of at least two year’s duration from the last FCR administration or beyond.”

- **The result of the vote was a majority in favor of not recommending funding.**
- **The Deputy Minister of Health has accepted both recommendations.**