FINAL RECOMMENDATION on RECONSIDERATION and REASONS for RECOMMENDATION

PEGFILGRASTIM
(Neulasta™—Amgen Canada Inc.)

Description
Pegfilgrastim (Neulasta™) is a long-acting formulation of filgrastim, a recombinant human granulocyte colony–stimulating factor. Pegfilgrastim is indicated to decrease the incidence of infection manifested by febrile neutropenia in patients with non-myeloid malignancies receiving myelosuppressive anti-neoplastic agents.

Recommendation
CEDAC recommends that pegfilgrastim be listed for patients with non-myeloid cancer who are receiving regimens with curative intent who are at high risk of developing prolonged neutropenia.

Reasons for recommendation
1. Five randomized controlled trials, available as full manuscripts, were reviewed. All compared pegfilgrastim with filgrastim in patients with non-myeloid malignancies receiving myelosuppressive anti-neoplastic agents. A systematic review came to the following conclusions:

   - In the studies that report these outcomes, there was no difference between the two formulations of filgrastim in mortality, hospitalization rates, development of serious neutropenia, median time to recovery of absolute neutrophil count, febrile neutropenia during a cycle of chemotherapy, rate of antibiotic use, dose intensity of chemotherapy, or adverse reactions.

   - Four of the five RCTs reported no statistically significant difference in the number of patients having febrile neutropenia in any single treatment cycle. One RCT also reported no statistically significant difference in the number of patients with febrile neutropenia during any treatment cycle, but reported a statistically significant difference in the number of patients with febrile neutropenia at some point in the study when all 4 treatment cycles were combined: 18% (27/147) and 9% (14/149) for filgrastim and pegfilgrastim, respectively (2-sided 95% CL -16.8% to -1.1%; P = 0.029).

   - Quality of Life, and time to resolution of fever were not reported in any of the studies.

   In summary, in head-to-head randomized trials, pegfilgrastim was not found to have a significant therapeutic advantage compared to filgrastim. The statistically significant reduction

in the prevalence of febrile neutropenia in one trial without associated clinical benefit was not considered sufficient evidence that pegfilgrastim offers a therapeutic advantage.

2. The Committee recognized that the once per-cycle dose of pegfilgrastim provides a patient comfort advantage over once-per-day filgrastim where several days of therapy are required.

3. The cost comparison between pegfilgrastim and filgrastim is made difficult by variable dosing of filgrastim across Canada. In some cases, patients are dispensed the vial that will provide their required dose, based on the indicated dosing of 5 microgram/kilogram; the remaining filgrastim is wasted, as partial vials cannot be saved. In other parts of the country, the 300 microgram vial of filgrastim is used regardless of patient weight. Communications with drug plans indicate that the use of the 300 microgram vial may exceed that of the 480 microgram vial. Pegfilgrastim is given as one dose for all adults–6 milligrams per treatment cycle without waste.

   The cost of pegfilgrastim relative to that of filgrastim varies considerably depending upon the patient, clinical practice, and local reimbursement policy. For example, if the 300-microgram vial of filgrastim is provided for eleven days, an average duration for a treatment cycle, the drug costs for one cycle are $1,810 for filgrastim versus $2,252 for pegfilgrastim--pegfilgrastim is $442 per cycle more expensive (or $1768 per four cycles of treatment). If a shorter course of filgrastim is used (e.g., 8 days), the cost difference becomes even greater. On the other hand, if the 480-microgram vial of filgrastim is used, the drug cost for eleven days of treatment with filgrastim is $2,897, while the cost of pegfilgrastim is $2,252. This works out to a cost saving of $645 per cycle with pegfilgrastim ($2,580 per treatment).

   The Committee concluded that, on average, the drug costs for pegfilgrastim are likely more than for filgrastim. However, this increase in drug costs will be partially offset by a decrease in the costs associated with the daily injections of filgrastim (although many patients inject themselves) and in patients with prolonged neutropenia in whom costs of pegfilgrastim may possibly be equal or less than those for filgrastim.

Of Note

1. The Committee had concerns about the cost effectiveness of pegfilgrastim, given its cost of approximately $9,000 per course of chemotherapy. Since filgrastim was the comparator used to assess the cost effectiveness of pegfilgrastim, the Committee recommends that the cost effectiveness of granulocyte colony stimulating factors should be reviewed as a “class”. Of interest to the committee is the impact of filgrastim on the proportion of patients receiving intravenous antibiotics, infection-related hospitalization, infection-related mortality, complete tumor response, overall hospitalization and overall survival.

2. Because pegfilgrastim and filgrastim are of similar efficacy, and the relative cost of the two drugs depends upon the dose and length of use of filgrastim, it is recommended that funding jurisdictions evaluate their current utilization of filgrastim.

3. Both published and unpublished data were reviewed and taken into consideration in making this recommendation.