



PGTM Clinical Intervention Model (CIM)
*Descriptive analysis of the pediatric use of filgrastim in
Quebec's university teaching hospitals (UTHs) - 2018*

Background: The introduction of granulocyte-colony stimulating factors into clinical oncology practice is clearly a major advance in cancer treatment. Used in primary and secondary prophylaxis, filgrastim has shown its ability to significantly reduce the duration of neutropenia and the risk of infection that can occur following myelosuppressive chemotherapy. However, as for the treatment of already-established febrile neutropenia (FN), while this might be an appealing idea, no clear data have confirmed any benefit in terms of infection-related mortality or patient survival that would justify prescribing filgrastim without well-defined risk factors.

Unlike the adult population, there is no guide for clinicians for managing FN in pediatric patients. There is no guide or list clearly specifying the universally recognized risk factors as there is for adults. The decision to use filgrastim is generally guided by the disease-specific clinical research trials conducted by the Children's Oncology Group (COG).

The PGTM's scientific recommendations

For the treatment of FEBRILE NEUTROPENIA:

- Locally ensure, preferably by means of a prospective drug utilization review (DUR), that the use of filgrastim for treating FN is optimized in accordance with the UTH's updated criteria. Special attention should be given to the duration of treatment.

For PRIMARY prophylaxis:

- For the most common diagnoses, review or create standing orders to assist in the prescribing of primary prophylaxis, based on pediatric study protocols, such as those of the COG. Assess the relevance of initiating filgrastim 48 hours after chemotherapy.
- When not indicated in the chemotherapy protocol, determine, on an ongoing basis, the risk of FN (high, moderate or low) associated with any new protocol, based on the scientific literature and the characteristics of the drugs in the protocol.

Other:

- Reassess the need to prescribe filgrastim and regulate its prescription for indications other than those approved in the product monograph (e.g., continue the current practice, which consists in restricting the prescribing of filgrastim or asking the Department of Pediatric Hematology/Oncology for its opinion on the prescribing of filgrastim, a special medical need request, etc.).
- Maintain daily absolute neutrophil count (ANC) monitoring to ensure an adequate duration of treatment.
- Standardize the choice of target ANC in order to harmonize the practices between the UTHs for determining when to stop administering filgrastim.



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Objective: To promote optimal filgrastim use in the UTHs that treat pediatric patients.

Intervention measures: Each institution is to determine which interventions apply to its situation and to make one or more of them priorities.

Timetable: Institute applicable measures at each UTH within 12 months of October 2018.

Intervention plan for the PGTM's pediatric filgrastim CIM:

1. Present the results to the Pharmacy and Therapeutics Committee and/or the Cancer/Oncology Subcommittee, if applicable, and to other committees concerned, if relevant.
2. Present the local results to the clinical practitioners concerned, specifically, pediatric hematologists/oncologists, pharmacists, critical care physicians, emergency physicians, pediatricians, etc.
3. Together with the pediatric hematologists/oncologists, develop a collaborative plan for monitoring inpatients' absolute neutrophil count so that a decision to continue or stop filgrastim therapy can be made and recorded in a timely manner and before the daily dose is prepared. This plan should apply to all the care units (including the emergency department), 7 days a week.
4. Together with the pediatric hematologists/oncologists, develop an algorithm/decision tree, which is to include the risk factors to be monitored, for justifying the use of filgrastim for already-established FN.
5. Improve the standing chemotherapy orders by indicating on them, as is done for the emetogenic potential, the risk of FN (low, moderate or severe). If the risk is moderate, the practitioner should indicate the risk identified on a line provided for this purpose on the order. If the risk is low, a note should mention that the use of filgrastim will need to be discussed.
6. Develop a standing order as soon as possible when a new chemotherapy drug or chemotherapy protocol is used.
7. Carry out a follow-up study, preferably in the form of a prospective drug utilization review (DUR), to verify if filgrastim is being prescribed in accordance with the inpatient FN algorithm (or with the criteria on the standing order specifying the potential risks to be identified).
8. Carry out a follow-up study, preferably in the form of a prospective drug utilization review, to verify if the use of filgrastim on the outpatient clinic medication orders is compliant for outpatient primary prophylaxis.
9. Require, on a case-by-case basis, a special medical need request when filgrastim is to be used for off-label indications, based on RAMQ criteria (e.g., afebrile neutropenia in inpatients or increasing outpatients' neutrophil count prior to chemotherapy).
10. Maintain a watch on filgrastim biosimilars (e.g., possible in-syringe stability data, the availability of vials) in order to recommend or not their use to the UTHs and to establish, if applicable, the conditions of use for the pediatric population. It should be noted that the Children's Oncology Group (COG) recognizes the use of filgrastim biosimilars and that their use is not deemed a violation of certain research protocols.