

## Growth Factors/Cytokines for White Blood Cells

Cytokine	Adult Dose	Pregnant Women
G-CSF or filgrastim ( <a href="#">Neupogen</a> )	<ul style="list-style-type: none"> <li>• Subcutaneous administration</li> <li>• 5 ug/kg/day via simple daily injection</li> <li>• Continued until absolute neutrophil count &gt; 1.0 x 10<sup>9</sup> cells/L</li> </ul>	Class C (Same as adults)
Pegylated G-CSF or pegfilgrastim ( <a href="#">Neulasta</a> )	<ul style="list-style-type: none"> <li>• 1 subcutaneous dose, 6 mg</li> </ul>	Class C (Same as adults)
GM-CSF or sargramostim ( <a href="#">Leukine</a> )	<ul style="list-style-type: none"> <li>• Subcutaneous administration</li> <li>• 250 ug/m<sup>2</sup>/day</li> <li>• Continued until absolute neutrophil count &gt; 1.0 x 10<sup>9</sup> cells/L</li> </ul>	Class C (Same as adults)

G-CSF = granulocyte colony-stimulating factor

GM-CSF = granulocyte-macrophage colony-stimulating factor

**General comments:**

- Prescribers are strongly urged to consult detailed information for each drug in the hyperlinks.
- Although the 3 drugs listed in the table above are FDA approved for the treatment of chemotherapy induced neutropenia, none is approved for radiation induced neutropenia.
  - No prospective randomized trials have proven the either the efficacy or long term safety of hematopoietic growth factors in humans exposed to radiation.
  - However, efficacy after radiation exposure has been observed with incidents involving small numbers of patients, as tracked by [REAC/TS](#), and in smaller clinical studies.
  - Evidence from **animal studies** indicates that outcomes may be improved if growth factors are administered as soon as possible after radiation exposure, and prior to the onset of neutropenia.

- In a mass casualty radiation event, procurement and use of these drugs from the [Strategic National Stockpile](#) would require a formal [Emergency Use Authorization](#). Off label use by individual clinicians might occur, but FDA still recommends an EUA. Incident managers will probably provide direction on this issue during a mass casualty event.
- General guidance on when to initiate treatment with growth factors
  - Initiation of treatment should be strongly considered for victims who develop an absolute neutrophil count of  $< 0.500 \times 10^9$  cells/L and are not already receiving growth factor.
  - In mass casualty events, some clinicians may suggest prophylactic use for victims likely to have been exposed to a whole body dose of  $\geq 2$  Gy instead of waiting for the onset of neutropenia. (See REMM [Exposure algorithm](#), and [Emergency Use Authorization](#))
- For pregnant women
  - Experts in biodosimetry must be consulted.
  - Any pregnant patient with exposure to radiation should be evaluated by a health physicist and maternal-fetal specialist for an assessment of risk to the fetus.
  - **Class C** refers to U.S. Food and Drug Administration Pregnancy Category C, which indicates that studies have shown animal, teratogenic, or embryocidal effects, but there are no adequate controlled studies in women; or no studies are available in animals or pregnant women.

**Additional issues/warning suggested by REMM consultants:**

- Safety and efficacy of growth factors in **pediatric patients** have not been established; however, available safety data for some of the growth factors (e.g., GM-CSF) indicate that this particular growth factor does not produce any greater toxicity in pediatric patients than in adults. [Emergency use authorization](#) would be required in a mass casualty event.
- Daily G-CSF (filgrastim and pegfilgrastim) therapy leads to splenic enlargement in a small majority of patients, and splenic rupture has been documented. Patients should avoid all but minimal left upper quadrant trauma (including abdominal palpation) for at least a week after G-CSF has been discontinued.
- Allergic reactions involving skin, respiratory, and cardiovascular symptoms have been reported in patients administered filgrastim and pegfilgrastim. Although

these have occurred at a relatively low rate (<1 in 4000 patients for filgrastim), in a large scale radiological incident there may be patients who experience this side effect.

- See practice guidelines for myeloid growth factors from
  - [National Comprehensive Cancer Network](#) (PDF - 178 KB)
  - [American Society of Clinical Oncology](#)