



Indiana Medicaid Therapeutics Committee **Therapeutic Class Review Summary**

Therapeutic Class:

Leukocyte (WBC) Stimulants

Overview:

The leukocyte stimulants are colony-stimulating factors (CSFs). CSFs are cytokines that are responsible for the regulation of hematopoiesis and certain activities of specific cell lines. Leukocyte stimulants have significantly impacted the supportive care of the immunocompromised patient, both clinically and economically. These agents have lessened the severity of myelosuppression, allowed chemotherapy dose intensification and/or maintenance of dose intensity, and reduced the duration of neutropenia and incidence of infection during selected chemotherapy regimens. However, to date, these agents have not demonstrated disease-free or overall survival benefit.

The three leukocyte stimulants on the US market are all products of recombinant technology. Filgrastim is recombinant human granulocyte colony-stimulating factor (rhuG-CSF) produced by *E. coli*. Pegfilgrastim is produced by covalently binding a 20-kiloDalton polyethylene glycol (PEG) molecule to the nitrogen terminus of filgrastim. Sargramostim is yeast-derived (*S. cerevisiae*) granulocyte-macrophage colony-stimulating factor (rhuGM-CSF).

Filgrastim and pegfilgrastim stimulate the production and maturation of neutrophil precursors and enhance the functions of mature neutrophils. Sargramostim is a multilineage growth factor that supports the survival and differentiation of progenitors in the granulocyte-macrophage lineage as well as megakaryotic and erythroid progenitor cells.

Filgrastim and sargramostim are indicated in induction chemotherapy of acute myeloid leukemia (AML), bone marrow transplant, peripheral blood progenitor cell (PBPC) collection and therapy, and severe chronic neutropenia (SCN). Filgrastim is also indicated in consolidation chemotherapy of AML and myelosuppressive chemotherapy. Filgrastim has been frequently studied and/or used in several other conditions for which it is not FDA-approved, including HIV-related neutropenia, severe community acquired pneumonia, severe rheumatoid arthritis, and diabetic foot infection. Sargramostim is also indicated in bone

marrow transplant failure or engraftment delay. Pegfilgrastim is indicated only in the treatment of chemotherapy-induced neutropenia. However, the polyethylene glycol molecule of pegfilgrastim increases its terminal half-life which confers the therapeutic advantage of allowing less frequent dosing.

Bone pain is the most common adverse event for all of the agents. Other adverse events associated with filgrastim and pegfilgrastim include headache, splenomegaly, anemia, thrombocytopenia, and dermatologic reactions. Sargramostim has been associated with peripheral edema, capillary leak syndrome, pleural and pericardial effusions, sequestration of granulocytes in the pulmonary system leading to dyspnea, and neutralizing antibody formation.

| Generic Name | Brand Name | Manufacturer | Generic Available |
|---------------------|-------------------|---------------------|--------------------------|
| Filgrastim | Neupogen® | Amgen | N |
| Pegfilgrastim | Neulasta™ | Amgen | N |
| Sargramostim | Leukine® | Berlex/Bayer | N |

Summary:

In clinical studies, pegfilgrastim and filgrastim have demonstrated equivalent efficacy. In some PBPC mobilization studies, filgrastim demonstrated superior efficacy over sargramostim. Due to the unique mechanism of action and high cost of recombinant leukocyte stimulants, the PDL process should entail ensuring these agents are provided to patients who will benefit from the treatment.