Hematopoietic Agents : Granulocyte Colony Stimulating Factors (G-CSF)

WA.PHAR.72 Hematopoietic Agents Granulocyte Colony Stimulating Factors (G-CSF) Effective Date: July 1, 2019

Note:

- *For non-preferred agents in this class/category, patients must have had an inadequate response or have had a documented intolerance due to severe adverse reaction or contraindication to at least TWO* preferred agents.*
  **If there is only one preferred agent in the class/category documentation of inadequate response to ONE preferred agent is needed*
- *If a new-to-market drug falls into an existing class/category, the drug will be considered non-preferred and subject to this class/category prior authorization (PA) criteria*

Background:

Granulocyte colony stimulating factor (G-CSF), or colony-stimulating factor 3, is a glycoprotein cytokine that stimulates formation of granulocyte colonies from the proliferation of a single hematopoietic stem cell. G-CSFs can be used to treat or prevent infections for patients with a low white cell count.

Filgrastim, a recombinant human G-CSF, increases the production of neutrophilic granulocytes in patients with chemotherapy-induced neutropenia and febrile neutropenia. Pegfilgrastim is a modified version of filgrastim that has an extended half-life and can work for a longer duration in the body and requires fewer administrations. However, pegfilgrastim has fewer approved uses than filgrastim.

Medical necessity:

Drug	Medical Necessity
filgrastim (Neupogen) filgrastim-aafi (Nivestym) filgrastim-sndz (Zarxio) tbo-filgrastim (Granix)	**Filgrastim** may be considered medically necessary when used to: • decrease the incidence of infection, as manifested by febrile neutropenia, in patients with nonmyeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a significant incidence of severe neutropenia with fever • reduce the time to neutrophil recovery and the duration of fever, following induction or consolidation chemotherapy treatment of patients with acute myeloid leukemia (AML) • reduce the duration of neutropenia and neutropenia-related clinical sequelae, e.g., febrile neutropenia, in patients with nonmyeloid malignancies undergoing myeloablative chemotherapy followed by bone marrow transplantation (BMT) • mobilize autologous hematopoietic progenitor cells into the peripheral blood for collection by leukapheresis • reduce the incidence and duration of sequelae of severe neutropenia (e.g., fever, infections, oropharyngeal ulcers) in symptomatic patients with congenital neutropenia, cyclic neutropenia, or idiopathic neutropenia

	• increase survival in patients acutely exposed to myelosuppresive doses of radiation (hematopoietic syndrome of acute radiation syndrome) **Filgrastim** is NOT considered medically necessary for: • Splenic rupture • Acute respiratory distress syndrome • Serious allergic reactions to pegfilgrastim • Sickle cell crisis • WBC count greater than 100 x 10^9/L (100,000 K/mL) or ANC greater than 10 x 10^9/L (10,000 K/mL) • Capillary leak syndrome • Aortitis • Cutaneous vasculitis • Within 24 hours before/after chemotherapy • Routine use as prophylaxis with chemotherapy regimens associated with low risk for febrile neutropenia • Routine use as prophylaxis with chemoradiation
pegfilgrastim (Neulasta) pegfilgrastim-cbqv (Udenyca) pegfilgrastim-jmdb (Fulphila) pegfilgrastim-bmez (Ziextenzo)	**Pegfilgrastim** may be considered medically necessary when used to: • Decrease the incidence of infection, as manifested by febrile neutropenia, in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a clinically significant incidence of febrile neutropenia. • Increase survival in patients acutely exposed to myelosuppressive doses of radiation (hematopoietic subsyndrome of acute radiation syndrome). **Pegfilgrastim** is NOT considered medically necessary for: • Mobilization of peripheral blood progenitor cells for hematopoietic stem cell transplantation • Splenic rupture • Acute respiratory distress syndrome • Serious allergic reactions to filgrastim • Sickle cell crisis • WBC count greater than 100 x 10^9/L (100,000 K/mL) or ANC greater than 10 x 10^9/L (10,000 K/mL) • Capillary leak syndrome • Aortitis • Cutaneous vasculitis • Within 24 hours after chemotherapy or with cytotoxic chemotherapy given more often than every 14 days • Routine use as prophylaxis with chemotherapy regimens associated with low risk for febrile neutropenia • Routine use as prophylaxis with chemoradiation

Clinical policy:

Indication	Clinical Criteria
Patients receiving induction and/or consolidation chemotherapy for AML	**Filgrastim** may be approved for patients set to receive induction or consolidation chemotherapy for acute myeloid leukemia (AML) If ALL the criteria are met, the request will be approved for 3 months.
Primary Prevention of febrile neutropenia in patients receiving myelosuppressive chemotherapy	**Filgrastim** may be approved for the primary prevention of febrile neutropenia if ONE (1, 2, or 3) of the following criteria is met or **pegfilgrastim** may be approved for the primary prevention of febrile neutropenia if ONE (1, 2 or 3) and 4 are met: 1. The chemotherapy regimen has a greater than 20% risk for febrile neutropenia; **OR** 2. The chemotherapy regimen has a 10 - 20% risk for febrile neutropenia and the member meets ONE of the following: a. Extensive prior chemotherapy or radiation therapy to pelvis or other areas important for bone marrow reserve b. Persistent neutropenia (ANC 1000/mm3 or less) c. Bone marrow involvement by tumor d. Recent surgery and/or open wounds e. Liver dysfunction (bilirubin > 2.0 mg/dL) f. Renal dysfunction (eGFR < 50 mL/min/1.73m^2) g. Age > 65 years and receiving full chemotherapy dose intensity h. Poor performance status 3. The member has experienced treatment delay of curative chemotherapy due to a dose-limiting neutropenic event, with the same dose and schedule planned for future cycles; OR **For pegfilgrastim only**: 4. Documented treatment failure or a clearly stated rational of an inability to complete course of treatment (e.g. patient is unable to administer daily injections, patient is a young child, etc.) with a preferred short-acting G-CSF If ALL the criteria are met, the request will be approved for 3 months.
Secondary Prevention of febrile neutropenia in patients receiving myelosuppressive chemotherapy	**Filgrastim** may be approved for the secondary prevention of febrile neutropenia if ONE (1, 2, or 3) of the following criteria is met or **pegfilgrastim** may be approved for the secondary prevention of febrile neutropenia if ONE (1, 2, or 3) and 4 are met: 1. The member has experienced febrile neutropenia with a previous cycle of similar chemotherapy, with the same dose and schedule planned for future cycles; OR 2. The member has experienced treatment delay of curative chemotherapy due to a dose-limiting neutropenic event, with the same dose and schedule planned for future cycles; OR

	3. The member has experienced treatment delay of palliative chemotherapy due to a dose-limiting neutropenic event, and dose reduction or a delay in frequency of subsequent chemotherapy cycles is not recommended **For pegfilgrastim only**: 5. Documented treatment failure or a clearly stated rational of an inability to complete course of treatment (e.g. patient is unable to administer daily injections, patient is a young child, etc.) with a preferred short-acting G-CSF If ALL the criteria are met, the request will be approved for 3 months.
Treatment of febrile neutropenia	**Filgrastim** may be approved for the treatment of febrile neutropenia if BOTH (1 and 2) of the following criteria are met: 1. The patient has been diagnosed with febrile neutropenia; **AND** 2. The patient has ONE or more of the following high-risk factors: a. age greater than 65 years; b. hospitalized for febrile neutropenia; c. sepsis syndrome; d. invasive fungal infection; e. clinically documented infection such as pneumonia; f. prolonged or profound neutropenia; g. history of prior episodes of febrile neutropenia If ALL the criteria are met, the request will be approved for 1 month.
Patients with cancer undergoing bone marrow transplantation	**Filgrastim** may be approved if BOTH (1 and 2) are met: 1. Filgrastim is administered at least 24 hours after: a. cytotoxic chemotherapy; **OR** b. bone marrow infusion; 2. CBC & platelet counts are monitored daily during neutrophil recovery. If ALL the criteria are met, the request will be approved for 3 months.
Patients undergoing autologous peripheral blood progenitor cell collection and therapy	**Filgrastim** may be approved if BOTH (1 and 2) are met: 1. Filgrastim is administered for at least 4 days before the first leukapheresis procedure; **AND** 2. Filgrastim is continued until the last leukapheresis. If ALL the criteria are met, the request will be approved for 3 months.
Patients with severe chronic neutropenia (SCN)	**Filgrastim** may be approved after confirmation of diagnosis of SCN by evaluating serial CBCs with differential and platelet counts, and evaluating bone marrow morphology and karyotype. Filgrastim can only be approved after confirmation of a correct diagnosis of SCN. If ALL the criteria are met, the request will be approved for 12 months.

Patients acutely exposed to myelosuppressive doses of radiation	**Filgrastim** or **pegfilgrastim** may be approved for hematopoietic subsyndrome of acute radiation syndrome when patients are exposed to lethal doses of total-body radiation, but not doses high enough to lead to certain death as a result of injury to other organs. This includes accidental or intentional total-body radiation of doses of 3 to 10 Gy. If ALL the criteria are met, the request will be approved for 1 month.

Dosage and quantity limits

Indication	Dose and Quantity Limits
Patients with cancer receiving myelosuppressive chemotherapy or induction and/or consolidation chemotherapy for AML	1. Filgrastim: a. Starting dose is 5 µg/kg/d, administered by subcutaneous injection or by intravenous infusion, rounded to nearest dosage size, up to 14 doses per month. 2. Pegfilgrastim: a. Limited to 1 dose per chemotherapy cycle b. 6 mg for patients >45 kg c. 4 mg for pediatric patients 31-44 kg d. 2.5 mg for pediatric patients 21-30 kg e. 1.5 mg for pediatric patients 10-20 kg f. 0.1 mg/kg for pediatric patients <10 kg
Patients with cancer undergoing bone marrow transplantation	1. 10 µg/kg/day given as an intravenous infusion. 2. Filgrastim is reduced to 5 µg/kg/d when ANC is greater than 1 x 10^9/L (1000 K/mL) for 3 consecutive days, then discontinued if ANC remains greater than 1 x 10^9/L (1000 K/mL) for 3 more consecutive days, then resumed at 5 µg/kg/d if ANC decreases to less than 1 x 10^9/L (1000 K/mL). 3. If ANC decreases to less than 1 x 10^9/L (1000 K/mL) during 5 µg/kg/d periods, filgrastim is increased to 10 µg/kg/d, then steps in #2 repeated.
Patients undergoing autologous peripheral blood progenitor cell collection and therapy	1. 10 µg/kg/day given as a subcutaneous injection.
Patients with severe chronic neutropenia (SCN)	1. Recommended starting dose is 6 µg/kg subcutaneous injection twice daily for congenital neutropenia. 2. Recommended starting dose is 5 µg/kg subcutaneous injection once daily for cyclic or idiopathic neutropenia.
Patients acutely exposed to myelosuppressive doses of radiation	1. Filgrastim: a. 10 µg/kg/day subcutaneous injection 2. Pegfilgrastim: a. Limited to 2 doses per radiation exposure

	b. 6 mg/dose for patients >45 kg c. 4 mg/dose for pediatric patients 31-44 kg d. 2.5 mg/dose for pediatric patients 21-30 kg e. 1.5 mg/dose for pediatric patients 10-20 kg f. 0.1 mg/kg/dose for pediatric patients <10 kg

Coding:

HCPCS Code	Description
J1442 NEUPOGEN	Injection, filgrastim (g-csf), excludes biosimilars, 1 microgram
J1447 GRANIX	Injection, tbo-filgrastim, 1 microgram
J2505 NEULASTA	Injection, pegfilgrastim, 6 mg
Q5101 ZARXIO	Injection, filgrastim (g-csf), biosimilar, 1 microgram
Q5108 FULPHILA	Injection, pegfilgrastim-jmdb, biosimilar (fulphila), 0.5 mg
Q5110 NIVESTYM	Injection, filgrastim-aafi, biosimilar, (nivestym), 1 microgram
C9058 ZIEXTENZO	Injection, pegfilgrastim-bemz, biosimilar (ziextenzo) 0.5 mg

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History

Date	Action and Summary of Changes
05/11/2020	Added Ziextenzo to policy
06/07/2019	Updated clinical criteria sections; updated approval duration sections
05/06/2019	New Policy