Medicare Advantage Medical Benefit Drug Policy

BlueCross BlueShield Nebraska

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Effective Date: 08/12/2021

Colony Stimulating Factors (CSFs)

Fulphila™ (pegfilgrastim-jmbd)
Granix® (tbo-filgrastim)
Leukine® (sargramostim)
Neulasta® (pegfilgrastim)
Neulasta On-Pro® (pegfilgrastim)
Neupogen® (filgrastim)
Nivestym™ (filgrastim-aafi)
Nyvepria™ (pegfilgrastim-apgf)
Udenyca™ (pegfilgrastim-cbqv)
Zarxio® (filgrastim-sndz)
Ziextenzo™ (pegfilgrastim-bmez)

FDA approval: Various
HCPCS: Fulphila – J3490, Granix – J1447, Leukine – J2820, Neupogen – J1442, Neulasta – J2505, Nivestym J3490, Nyvepria - Q5122, Udenyca – Q5111, Zarxio – J3490, Zietxenzo – Q5120, C9058
Benefit: Both

Policy:

Requests must be supported by submission of chart notes and patient specific documentation.

A. Coverage of the requested drug is provided for FDA approved indications and when all the following are met:
   a. Primary prophylaxis of chemotherapy-induced febrile neutropenia is considered clinically appropriate when ALL of the following are met:
      i. The individual has a non-myeloid malignancy
      ii. Chemotherapy intent must include one of the following:
         1. Curative intent (adjuvant treatment for early stage disease, for example)
            OR
         2. Intent is survival prolongation, and the use of a different regimen or dose reduction would reduce the likelihood of reaching the treatment goal
            OR
         3. Intent is symptom management, and the use of a different regimen or dose reduction would reduce the likelihood of reaching the treatment goal
      iii. The individual falls into one of the following risk categories for febrile neutropenia:
         1. High risk of febrile neutropenia (≥ 20%) based on chemotherapy regimen
            OR

2. Intermediate risk of febrile neutropenia (≥ 10% but < 20%) based on chemotherapy regimen, and at least ONE of the following significant risk factors:
    a) Age > 65
    b) Poor performance status (ECOG 3 or 4, but chemotherapy still indicated)
    c) Preexisting neutropenia, for example resulting from bone marrow damage or tumor infiltration (ANC < 1500 mm^3)
    d) Previous febrile neutropenia episode from a prior treatment regimen
    e) Liver dysfunction, with bilirubin ≥ 1.0 or liver enzymes ≥ 2x upper limit of normal
    f) Presence of open wounds or active infections, when chemotherapy cannot be delayed to accommodate recovery
    g) Renal dysfunction with creatinine clearance of less than 50 mL/min
    h) Poor nutritional status (baseline albumin less ≤ 3.5 g/dL or BMI less than 20)
    i) HIV infection
    j) Advanced cancer (i.e. metastatic or stage IV, unresectable disease).
    k) Multiple (5 or more) chronic conditions or at least two serious comorbidities

b. Secondary prophylaxis of febrile neutropenia is considered clinically appropriate when there has been a previous neutropenic complication (in the absence of primary prophylaxis), and a change to the regimen (including dose reduction, schedule change, or change in therapy) would be expected to compromise patient outcome, particularly in the setting of curative intent.
c. Adjunctive treatment of febrile neutropenia is considered clinically appropriate when any of the following risk factors are present
    i. Age > 65
    ii. Neutrophil recovery is expected to be delayed (greater than 10 days)
    iii. Neutropenia is profound (less than 0.1 x 10^9)
    iv. Active pneumonia
    v. Sepsis syndrome (hypotension and/or multi-organ damage/dysfunction noted)
    vi. Invasive fungal or opportunistic infection
    vii. Onset of fever during inpatient stay
d. The following indications by growth factor type are also considered clinically appropriate when the requirements below are met:
    i. Filgrastim and filgrastim biosimilars
        1. Acute lymphocytic leukemia (ALL)
            a) After start of induction or first post-remission chemotherapy course;
            OR
            b) As an alternate or adjunct to donor leukocyte infusions (DLI) for relapsed disease after transplant
        2. Acute myeloid leukemia (AML)
            a) After induction, reinduction, or consolidation;
            OR
            b) As an alternate or adjunct to donor leukocyte infusions (DLI) for relapsed disease after transplant
        3. Aplastic anemia, moderate or severe
        4. To treat severe neutropenia in hairy cell leukemia
        5. Hematopoietic stem cell transplant
            a) To promote bone marrow myeloid recovery;
            OR
            b) To treat delayed or failed engraftment;
            OR
            c) To mobilize stem cells for collection by pheresis
        6. Myelodysplastic syndrome (MDS)
            a) To treat recurrent infection;
            OR

b) To treat neutrophil count < 500 mm^3

7. Radiation exposure
    a) Following radiation therapy in the absence of chemotherapy, if prolonged delays are expected;
    OR
    b) After accidental or intentional body irradiation of doses greater than 2 Gy (hematopoietic syndrome of acute radiation syndrome)
8. Support for dose dense or dose intensive chemotherapy in any of the following scenarios:
    a) Adjuvant treatment of high-risk breast cancer with combination therapy that includes anthracycline (doxorubicin or epirubicin)/cyclophosphamide followed by paclitaxel;
    OR
    b) High-dose intensity methotrexate, vinblastine, doxorubicin, and cisplatin (HD-M-VAC) in urothelial cancer;
    OR
    c) Chemotherapy intensification for newly diagnosed, localized Ewing sarcoma

ii. Peg-filgrastim and peg-filgrastim biosimilars
1. Acute lymphocytic leukemia (ALL) after the start of induction of first post-remission chemotherapy course
2. Hematopoietic stem cell transplant
    a) To promote bone marrow myeloid recovery;
    OR
    b) To treat delayed or failed engraftment
3. Myelodysplastic syndrome (MDS)
    a) To treat recurrent infection;
    OR
    b) To treat neutrophil count < 500 mm^3
4. After accidental or intentional body irradiation of doses greater than 2 Gy (hematopoietic syndrome of acute radiation syndrome)
5. Support for dose dense chemotherapy in any of the following scenarios:
    a) Adjuvant treatment of high-risk breast cancer with combination therapy that includes anthracycline (doxorubicin or epirubicin)/cyclophosphamide followed by paclitaxel;
    OR
    b) High-dose intensity methotrexate, vinblastine, doxorubicin, and cisplatin (HD-M-VAC) in urothelial cancer;
    OR
    c) Chemotherapy intensification for newly diagnosed, localized Ewing sarcoma

iii. Sargramostim
1. Acute lymphocytic leukemia (ALL) after the start of induction or first post-remission chemotherapy course
2. Acute myeloid leukemia (AML) after induction, reinduction, for individuals over 55 years of age
3. Hematopoietic stem cell transplant
    a) To promote bone marrow myeloid recovery;
    OR
    b) To treat delayed or failed engraftment;
    OR
    c) To mobilize stem cells for collection by pheresis
4. Myelodysplastic syndrome (MDS)
    a) To treat recurrent infection;
    OR
    b) To treat neutrophil count < 500 mm^3
5. Radiation exposure

a) After radiation therapy in the absence of chemotherapy, if prolonged delays are expected;
OR
b) After accidental or intentional body irradiation of doses greater than 2 Gy (hematopoietic syndrome of acute radiation syndrome)

6. Support for dose dense chemotherapy in any of the following scenarios:
a) Adjuvant treatment of high-risk breast cancer with combination therapy that includes anthracycline (doxorubicin or epirubicin)/cyclophosphamide followed by paclitaxel;
OR
b) High-dose intensity methotrexate, vinblastine, doxorubicin, and cisplatin (HD-M-VAC) in urothelial cancer
OR
c) Chemotherapy intensification for newly diagnosed, localized Ewing sarcoma

iv. Tbo-filgrastim for use in hematopoietic stem cell transplant in any of the following scenarios:
1. To promote bone marrow myeloid recovery;
OR
2. To treat delayed or failed engraftment;
OR
3. To mobilize stem cells for collection by pheresis

e. Trial and failure, contraindication, OR intolerance to the preferred drugs as listed in BCBSNE Part B drugs prior authorization list

B. Quantity Limitations, Authorization Period and Renewal Criteria
a. Quantity Limit: Align with FDA approved dosing
b. Initial Authorization Period: 1 year
c. Renewal Criteria: Authorization may be reviewed at least annually to confirm that current criteria are met and that the medication is effective as demonstrated by a decrease in the interruption of chemotherapy cycles and reduced incidence of febrile neutropenia
d. Renewal Authorization Period: 1 year

***Note: Coverage may differ for Medicare Part B members based on any applicable criteria outlined in Local Coverage Determinations (LCD) or National Coverage Determinations (NCD) as determined by Center for Medicare and Medicaid Services (CMS). See the CMS website at http://www.cms.hhs.gov/. Determination of coverage of Part B drugs is based on medically accepted indications which have supported citations included or approved for inclusion determined by CMS approved compendia.

Therapeutic considerations:

A. **FDA approved indication/Diagnosis**

**Please refer to most recent prescribing information.*

B. **Background Information**

a. There are different types of colony stimulating factors (CSFs). Filgrastim-products, pegfilgrastim products and Leukine is the only sargramostim product. Filgrastim and pegfilgrastim products are human granulocyte colony-stimulating factors (G-CSFs). Leukine is a human granulocyte-macrophage CSF (GM-CSF).

b. Filgrastim products

i. Granix is FDA approved to reduce the duration of severe neutropenia in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer medications associated with a clinically

significant incidence of febrile neutropenia. It is not technically considered a biosimilar because it was filed as a Biologics License Application since a biosimilars approval pathway had not been established at the time of FDA submission.

ii. Neupogen is approved to:

1. Decrease the incidence of infection, as manifested by febrile neutropenia, in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a significant incidence of severe neutropenia and fever.

2. Reduce the time to neutrophil recovery and the duration of fever following induction or consolidation chemotherapy treatment of adults with AML.

3. Reduce the duration of neutropenia and neutropenia-related clinical sequelae (e.g., febrile neutropenia) in patients with non-myeloid malignancies undergoing myeloablative chemotherapy followed by BMT.

4. Mobilization of autologous hematopoietic progenitor cells into the peripheral blood for collection by leukapheresis.

5. Chronic administration to reduce the incidence and duration of sequelae of neutropenia in symptomatic patients with congenital neutropenia, cyclic neutropenia, or idiopathic neutropenia.

6. Increase survival in patients acutely exposed to myelosuppressive doses of radiation (hematopoietic syndrome of acute radiation syndrome).

iii. All of Neupogen's biosimilars are approved for the same indications as Neupogen with the exception of use to increase survival in patients acutely exposed to myelosuppressive doses of radiation (hematopoietic syndrome of acute radiation syndrome). That indication is protected by Orphan Drug Exclusivity until March 30, 2022.

c. Pegfilgrastim products

i. Neulasta is approved to

1. 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. Limitation of Use: This agent is not indicated for mobilization of peripheral blood progenitor cells for HSCT.

2. Increase survival in patients acutely exposed to myelosuppressive doses of radiation (hematopoietic subsyndrome of acute radiation syndrome).

ii. All of Neulasta' s biosimilars are approved for the same indications as Neulasta with the exception of increasing survival in patients acutely exposed to myelosuppressive doses of radiation, which is protected by Orphan Drug Exclusivity until November 2022.

d. Sargramostim is approved

i. To shorten time to neutrophil recovery and to reduce the incidence of severe, life-threatening or fatal infections following induction chemotherapy in adult patients ≥ 55 years of age with AML.

ii. In adult patients with cancer undergoing autologous hematopoietic stem cell transplantation for the mobilization of hematopoietic progenitor cells into peripheral blood for collection by leukapheresis.

iii. To accelerate myeloid reconstitution following autologous peripheral blood progenitor cell or bone marrow transplantation in adult and pediatric patients ≥ 2 years of age with non-Hodgkin's lymphoma, lymphoblastic leukemia, and Hodgkin's lymphoma.

iv. For acceleration of myeloid reconstitution in adult and pediatric patients ≥ 2 years of age undergoing allogeneic bone marrow transplantation from HLA-matched related donors.

v. Treatment of adult and pediatric patients ≥ 2 years of age who have undergone allogeneic or autologous BMT in whom neutrophil recovery is delayed or failed.

vi. To increase survival in adult and pediatric patients from birth to 17 years of age acutely exposed to myelosuppressive doses of radiation (hematopoietic syndrome of acute radiation syndrome).

e. CSF products have an established role in the management of patients with non-myeloid malignancies who are receiving myelosuppressive anti-cancer agents, as well as for several other uses. Many studies have shown that the prophylactic use of these products reduces the incidence, duration, and severity of febrile neutropenia, decrease the subsequent rates of infection and hospitalization, and improves the delivery of full-dose intensity chemotherapy on schedule in patients with various cancers.

f. The National Comprehensive Cancer Network (NCCN) guidelines for various cancer and myeloid growth factors provides recommendations on the use of these agents. The criteria reflects these recommendations along with expert opinion.

g. Regarding biosimilars, the NCCN guidelines state an FDA approved biosimilar is an appropriate substitution for its reference products.

C. **Efficacy**

**Please refer to most recent prescribing information.*

D. **Medication Safety Considerations**

**Please refer to most recent prescribing information.*

E. **Dosing and administration**

**Please refer to most recent prescribing information.*

F. **How supplied**

**Please refer to most recent prescribing information.*

References:

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Policy History		
#	Date	Change Description
1.1	Effective Date: 08/12/2021	Annual review performed, no changes to criteria
1.0	Effective Date: 08/13/2020	Medical policy established.

** The prescribing information for a drug is subject to change. To ensure you are reading the most current information it is advised that you reference the most updated prescribing information by visiting the drug or manufacturer website or http://dailymed.nlm.nih.gov/dailymed/index.cfm.*