Neupogen

Description

Neupogen (filgrastim)

Background

Neupogen is a man-made form of granulocyte colony-stimulating factor (G-CSF), which is made using the bacteria Escherichia coli. G-CSF is a substance naturally produced by the body. It stimulates the growth of neutrophils, a type of white blood cell important in the body’s fight against infection (1).

Regulatory Status

FDA-approved indications:

1. **Cancer Patients Receiving Myelosuppressive Chemotherapy**
   Neupogen is indicated to decrease the incidence of infection, as manifested by febrile neutropenia, in patients with nonmyeloid malignancies receiving myelosuppressive anticancer drugs associated with a significant incidence of severe neutropenia with fever (1).

2. **Patients With Acute Myeloid Leukemia Receiving Induction or Consolidation Chemotherapy**
   Neupogen is indicated for reducing the time to neutrophil recovery and the duration of fever, following induction or consolidation chemotherapy treatment of adults with AML (1).
3. **Cancer Patients Receiving Bone Marrow Transplant**
Neupogen is indicated to reduce the duration of neutropenia and neutropenia-related clinical sequelae, e.g., febrile neutropenia, in patients with nonmyeloid malignancies undergoing myeloablative chemotherapy followed by marrow transplantation (1).

4. **Patients Undergoing Peripheral Blood Progenitor Cell Collection and Therapy**
Neupogen is indicated for the mobilization of hematopoietic progenitor cells into the peripheral blood for collection by leukapheresis (1).

5. **Patients with Severe Chronic Neutropenia**
Neupogen is indicated for chronic administration to reduce the incidence and duration of sequelae of neutropenia (e.g., fever, infections, oropharyngeal ulcers) in symptomatic patients with congenital neutropenia, cyclic neutropenia, or idiopathic neutropenia (1).

6. **Increase survival in patients acutely exposed to myelosuppressive doses of radiation**
(Hematopoietic Syndrome of Acute Radiation Syndrome) (1).

**Off-label Use**

Neutropenia secondary to anti rejection medications post transplant (9). A study by Hornedo determined the role of granulocyte colony stimulating factor (G-CSF) following transplantation in the post-transplant period. Patients receiving G-CSF reached 500 and 1,000 neutrophils significantly faster (P=0.001) than patients with no G-CSF. G-CSF accelerates the time to neutrophil engraftment. This translated into a significantly (P<0.05) shorter hospitalization time for patients receiving G-CSF (2). In kidney and liver transplant recipients, granulocyte colony-stimulating factor has been used successfully to reverse ganciclovir-induced neutropenia or cytomegalovirus-induced neutropenia (3).

Splenic rupture, including fatal cases, can occur following the administration of Neupogen. Patients who report left upper abdominal or shoulder pain after receiving Neupogen should be evaluated for an enlarged spleen or splenic rupture (1).

Acute respiratory distress syndrome (ARDS) can occur in patients receiving Neupogen or Zarxio. Patients should be evaluated for ARDS if they develop fever and lung infiltrates or respiratory distress after receiving Neupogen and should be discontinued in patients with ARDS (1).
Serious allergic reactions, including anaphylaxis, can occur in patients receiving Neupogen. The majority of reported events occurred upon initial exposure. Allergic reactions, including anaphylaxis, can recur within days after the discontinuation of initial anti-allergic treatment. Permanently discontinue therapy in patients with serious allergic reactions. Do not administer Neupogen to patients with a history of serious allergic reactions to pegfilgrastim or filgrastim (1). Neupogen should not be given in the period 14 days within receiving Neulasta (10).

Severe sickle cell crises can occur in patients with sickle cell disorders receiving Neupogen. Severe and sometimes fatal sickle cell crises can occur in patients with sickle cell disorders receiving filgrastim (1).

Related policies
Granix, Leukine, Neulasta, Zarxio

Policy
This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Neupogen may be considered medically necessary for the indications listed below. Neupogen may be considered investigational for all other indications.

Prior-Approval Requirements

Diagnoses
Patient must have ONE of the following:

1. Acute myeloid leukemia (AML)
   a. Following induction chemotherapy or consolidation chemotherapy
2. Agranulocytosis
3. Hematopoietic stem cell transplantation
4. Umbilical Cord Stem Cell Transplantation
5. Aplastic anemia
6. Hairy cell leukemia
7. Myelodysplastic syndrome in neutropenic patients with recurrent or resistant infections
8. Neutropenia
a. AIDS associated
b. Chemotherapy associated; prophylaxis in patients at intermediate to high risk for febrile neutropenia following chemotherapy with solid or non-myeloid malignancies
c. Hepatitis C therapy associated (ANC < 750mm$^3$)
d. Chronic Congenital (Kostmann’s Syndrome)
e. Cyclic neutropenia
f. Idiopathic neutropenia
g. Secondary to anti-rejection medications post-transplant
h. Ganciclovir-induced neutropenia
i. Cytomegalovirus-induced neutropenia
9. Peripheral blood progenitor cell (PBPC) collection
   a. Autologous peripheral blood progenitor cell (PBPC) mobilization and following transplantation
10. Hematopoietic Syndrome of Acute Radiation Syndrome

AND the following
1. **NOT** used in combination with another granulocyte colony-stimulating factor (G-CSF)

**Prior – Approval Renewal Requirements**
Same as above

**Policy Guidelines**

**Pre - PA Allowance**
None

**Prior - Approval Limits**

| Duration | Neupogen | 6 months |

**Prior – Approval Renewal Limits**

| Duration | Neupogen | 6 months |

**Rationale**
Summary
Filgrastim (Neupogen) is a recombinant human granulocyte-macrophage colony stimulating factor (rhu G-CSF) produced by Eschericoli coli (E coli) bacteria. It is FDA approved for use in myelosuppressive chemotherapy, AML receiving chemotherapy, bone marrow transplant, harvesting of peripheral blood stem cells and severe chronic neutropenia (1).

Prior authorization is required to ensure the safe, clinically appropriate and cost effective use of Neupogen while maintaining optimal therapeutic outcomes.

References
ICD-9 code was removed for myelosuppressive chemotherapy, to decrease the incidence of infection as manifested by febrile neutropenia (various), bone marrow transplantation (996.85), peripheral blood progenitor cell collection (various), acceleration of myeloid recovery in patients with non-Hodgkin’s lymphoma, ALL or Hodgkin’s disease undergoing bone marrow transplantation (various), induction chemotherapy in acute myelogenous leukemia (various), mobilization and following transplantation of autologous PBPC (various), myeloid reconstitution after allogenic bone marrow transplantation (various), severe chronic neutropenia (various) and bone marrow transplantation failure or engraftment delay (996.0-996.5). ICD-9 code was updated for bone marrow transplantation failure or engraftment delay (996.82). ICD-10 code was added for bone marrow transplantation failure or engraftment delay (T86.02).

December 2010: Simplify criterion; listing approved diagnoses in a bullet point style which is easier to read with associated lab values supported in the FDA approved packaging. Removal of Neulasta from the colony stimulating agents PA criteria due to different FDA approved indications (1). Removal of remaining ICD-9 codes due to various codes used to indicate these diagnoses.

September 2011: Separating the colony stimulating agent criterion into individual agents; adding coverage for drug (non-chemotherapy) associated neutropenia for Hepatitis C treatment. Hepatitis C virus (HCV) therapy-induced neutropenia; defined as absolute neutrophil count (ANC) below 750 cells/µL. ANC typically decreases by 30-50% from normal with HCV therapy. Therefore, neutropenia is a common reason for dose reduction or withdrawal from HCV therapy (1). Treatment for neutropenia is granulocyte colony stimulating factors (G-CSF) such as Leukine. Several studies have shown that administration of G-CSF is effective in increasing neutrophil count and reducing dose reduction or withdrawal from HCV therapy, which leads to increased sustained virological response (SVR) (4,5). Not having to modify the dose of HCV therapy and an increased SVR means an improvement in the quality of life of the patient (5). Current criterion allows
for treatment of AIDS associated neutropenia supported by the FDA orphan drug status approved September 3, 1991 (6). Chemotherapy associated neutropenia is supported by the American Society of Clinical Oncology (ASCO), and National Comprehensive Cancer Network (NCCN) (7,8). Although not FDA approved; treatment of Myelodysplastic syndrome is supported by the American Society of Clinical Oncology (ASCO) and National Comprehensive Cancer Network (NCCN) (7,8). Agranulocytosis, aplastic anemia, and the use in hairy cell leukemia is supported by Micromedex (9).

January 2012  Added >50 for AML; clarified ANC requirements for neutropenia.
December 2012 Annual editorial review
March 2014 Annual editorial review and reference update, clarified age requirement for AML to be 18 years of age and older, added cyclic and idiopathic forms of neutropenia (1), added neutropenia secondary to anti rejection medications post transplant (9). Decreased approval and renewal limits to 6 months
March 2015 Annual editorial review and reference update
Addition of not used in combination with another granulocyte colony-stimulating factor (G-CSF)
April 2015 Addition of Zarxio to PA
June 2015 Removal of Zarxio from Neupogen criteria and addition of new indication
Hematopoietic Syndrome of Acute Radiation Syndrome
September 2015 Annual review
Removal of 18 years of age and older from the AML

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on September 18, 2015 and is effective October 1, 2015.

Deborah M. Smith, MD, MPH