Premier Health Plan

POLICY AND PROCEDURE

POLICY TITLE: **Granulocyte Colony-Stimulating Factors**
DEPARTMENT: **Clinical Pharmacy Services- Utilization Management**
ORIGINAL DATE: ***October 2005 (as adopted from UPMC Health Plan)***

Last P & T Committee Approval Date: *May 2018*

Product Applicability: *mark all applicable products below:*

COMMERCIAL	[ ] HMO [ ] PPO *Products*: [ ] Small [ ] Indiv. [ ] Large *Exchange*: [ ] Shop [ ] Indiv. [x] All
OTHER	[x] Self-funded/ASO

PURPOSE

The purpose of this policy is to define the prior authorization process for Granulocyte Colony-Stimulating Factors.

Filgrastim (Neupogen) and Filgrastim-sndz (Zarxio) are indicated:

- To decrease the incidence of infection, as manifested by febrile neutropenia (FN), in patients with nonmyeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a significant incidence of severe neutropenia with fever
- To reduce the time to neutrophil recovery and the duration of fever following induction or consolidation chemotherapy treatment of adults with Acute Myeloid Leukemia (AML)
- To reduce the duration of neutropenia-related clinical sequelae, e.g. FN, in patients with nonmyeloid malignancies undergoing myeloablative chemotherapy followed by marrow transplantation
- For the mobilization of hematopoietic progenitor cells into the peripheral blood for collection by leukophoresis

- For chronic administration to reduce the incidence and duration of sequelae of neutropenia (eg. fever, infections, oropharyngeal ulcers) in symptomatic patients with congenital neutropenia, cyclic neutropenia, or idiopathic neutropenia

Pegfilgrastim (Neulasta) is indicated for the following:

- To decrease the incidence of infection, as manifested by FN, in patients with nonmyeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a clinically significant incidence of febrile neutropenia

Sargramostin (Leukine) is indicated:

- For the use following induction chemotherapy in older adult patient with acute myelogenous leukemia (AML) to shorten time to neutrophil recovery and to reduceincidenceof severe and life-threatening infections and infections resulting in death
- For the mobilization of hematopoietic progenitor cells into peripheral blood for collection by leukapheresis
- For acceleration of myeloid recovery in patients with non-Hodgkin's lymphoma (NHL), acute lymphoblastic leukemia (ALL) and Hodgkin's disease undergoing autologous bone marrow transplantation (BMT)
- For acceleration of myeloid recovery in patients undergoing allogeneic BMT from HLA-matched related donors
- In patients who have undergone allogeneic or autologous BMT in whom engraftment is delayed or has failed
- 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 [H-ARS])

Tbo-filgrastim (Granix) is indicated:

- For reduction in the duration of severe neutropenia in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a clinical significant incidence of febrile neutropenia.

DEFINITIONS

CHOP – a chemotherapy regimen consisting of the following agents: cyclophosphamide, doxorubicin, vincristine, and prednisone.

Neutropenia – a reduction in the blood neutrophil count. Neutrophils represent 40-70% of the total white blood cell count and serve as the primary defense against infection.

The absolute neutrophil count is calculated via the following equation:
Absolute Neutrophil Count (ANC): Total white blood cell count (cells/µL) x % (neutrophils + bands). Bands represent immature neutrophils.

The severity of neutropenia relates to the relative risk of infection:

- Mild (ANC = 1000 – 1500/µL)
- Moderate (ANC = 500 – 1000/uL)
- Severe (ANC < 500/µL)

POLICY

It is the policy of the Health Plan to maintain a prior authorization process that promotes appropriate utilization of specific drugs with potential for misuse or limited indications. This process involves a review using Food and Drug Administration (FDA) criteria to make a determination of Medical Necessity, as defined in CRM.015-Medical Necessity, and approval by the Pharmacy & Therapeutics Committee of the criteria for prior authorization, as described in RX.003-Prior Authorization Process.

The drugs, filgrastim (Neupogen), filgrastin-sndz (Zarxio), pegfilgrastim (Neulasta), sargramostim (Leukine®), and tbo-filgrastim (Granix™) are subject to the prior authorization process.

PROCEDURE

Initial Authorization Criteria:

I. PLAN DESIGN SUMMARY

Requests for Neupogen, Granix, and Leukine are subject to the preferred medical drug list program. This program applies to the colony stimulating factor products specified in this policy. Coverage for non-preferred products is provided based on clinical circumstances that would exclude the use of the preferred product and may be based on previous use of a product. The coverage review process will ascertain situations where a clinical exception can be made. This program applies to all members requesting treatment with a non-preferred product.

Each referral is reviewed based on all utilization management (UM) programs implemented for the client.

Table. Colony Stimulating Factors

	Product(s)
Preferred	• Zarxio (filgrastim-sndz)
Non-preferred	• Neupogen (filgrastim) • Granix (TBO-filgrastim) • Leukine (sargramostim)

Requests for a non-preferred drug must meet one of the following exception criteria in addition to clinical criteria:

II. EXCEPTION CRITERIA (*Use for Neupogen/Granix/Leukine Requests Only*)

A. Coverage for the non-preferred products, Neupogen or Granix, is provided when the member meets one of the following criteria:
   1. The member had a documented previous treatment failure or an intolerable adverse event to Zarxio.
   2. The member has a documented latex allergy and the prescriber states that the member must use latex-free vials.
   3. Neupogen or Granix are requested for doses less than 180 mcg.

B. Coverage for the non-preferred product, Leukine, is provided when the member meets one of the following criteria:
   1. Leukine will be used for myeloid reconstitution after autologous or allogenic bone marrow transplant or bone marrow transplant engraftment delay or failure.
   2. Leukine will be used 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 [H-ARS])
   3. The member had a documented previous treatment failure or an intolerable adverse event to Zarxio.

III. CLINICAL CRITERIA (*Use for ALL Drug Requests*)

Must meet all of the clinical criteria listed under the respective drug product:

1. For filgrastim (Neupogen), filgrastim-sndz (Zarxio), and tbo-filgrastim (Granix):
- For primary prophylaxis of FN, must have one of the following:

  - Must have a solid tumor or non-myeloid malignancy and be receiving myelosuppressive chemotherapy which has a greater than 20% risk of FN, as calculated in current American Society of Clinical Oncology (ASCO) and National Comprehensive Cancer Network (NCCN) guidelines for myeloid growth factors
  - Must have a solid tumor or non-myeloid malignancy, be receiving nonmyelosuppressive chemotherapy which has ≤ 20% risk of FN, and be considered to be at high risk for chemotherapy-induced FN or infection due to *at least one* of the following
    - Age greater than 65 years
    - Poor performance status
    - Previous episode of FN
    - Extensive prior treatment including large radiation ports
    - Previous chemotherapy or radiation therapy
    - Preexisting neutropenia
    - Cytopenias due to bone marrow involvement by tumor
    - Poor nutritional status
    - Presence of open wounds or active infections
    - Recent surgery
    - Advanced cancer
    - Poor renal function
    - Liver dysfunction, most notably elevated bilirubin
    - Other serious comorbidities
  - Must be receiving a dose-dense chemotherapy regimen for the treatment of node-positive breast cancer, small-cell lung cancer, or diffuse aggressive non-Hodgkin's Lymphoma
- For secondary prophylaxis of FN:
  - Must have experienced a neutropenic complication from a prior cycle of chemotherapy for which primary prophylaxis was not received, in which a reduced dose may compromise disease-free or overall survival or treatment outcome
- For treatment of febrile patients with neutropenia:
  - Must have fever and neutropenia and be at high-risk for infection-related complications, or have prognostic factors that are predictive of poor clinical outcomes. Must have *at least one* of the following high-risk features:
    - Sepsis syndrome
    - Expected prolonged (> 10 days) neutropenia
    - Severe neutropenia with ANC < 100/µL
    - Age greater than 65 years

        - Uncontrolled primary disease
        - Pneumonia
        - Hypotension and multi-organ dysfunction (sepsis syndrome)
        - Invasive fungal infection
        - Other clinically documented infections
        - Being hospitalized at time of fever
        - Prior episode of febrile neutropenia
    - Must **NOT** have received prophylactic pegfilgrastim (Neulasta) during current chemotherapy cycle

2. For filgrastin (Neupogen) and filgrastin-sndz (Zarxio) only:

- For use in bone marrow transplant, must have one of the following:
    - Must require administration after *autologous* (not allogeneic) peripheral blood progenitor cell (PBPC) transplant
    - Must require mobilization of progenitor cells into peripheral blood, often in conjunction with chemotherapy, for collection by leukophoresis.
- For use in Acute Myeloid Leukemia (AML):
    - Must be an adult with a diagnosis of AML receiving induction or consolidation therapy
- For use in Acute Lymphocytic Leukemia (ALL):
    - Must have a diagnosis of ALL after completion of the initial first few days of chemotherapy of the initial induction or first post-remission course
- For use in Myelodysplastic Syndromes (MDS):
    - Must have a diagnosis of MDS, severe neutropenia, and recurrent infection
- For use in patients receiving radiation:
    - Must be receiving radiation therapy, without concomitant chemotherapy, and have expected prolonged delays secondary to neutropenia
- For use in older lymphoma patients:
    - Must be age 65 years and older with a diagnosis of acute aggressive lymphoma treated with curative chemotherapy (CHOP or more aggressive regimens)
- For use in congenital, cyclic, or idiopathic neutropenia:
    - Must have a diagnosis of congenital, cyclic, or idiopathic neutropenia with symptompatic neutropenia
- For use in drug-induced agranulocytosis:
    - Must have severe neutropenia associated with fever or evidence of serious infection as a result of myelosuppressive medication
- For use in patients patients acutely exposed to myelosuppressive doses of radiation (Hematopoietic Syndrome of Acute Radiation Syndrome)

- Must have been exposed to lethal doses of total-body radiotherapy, but not doses high enough to lead to certain death due to injury to other organs

3. For pegfilgrastim (Neulasta):

- For primary prophylaxis of FN
  - Must be receiving a chemotherapy regimen with a dosing frequency of once every 2 weeks or greater
  - Must have one of the following:
    - Must be receiving myelosuppressive chemotherapy which has a greater than 20% risk of FN (as calculated in current ASCO and NCCN guidelines for myeloid growth factors)
    - Must be receiving non-myelosuppressive chemotherapy which has ≤20% risk of FN and be considered to be at high risk for chemotherapy-induced FN or infection due to at least one of the following:
      - Age greater than 65 years
      - Poor performance status
      - Previous episode of FN
      - Extensive prior treatment including large radiation ports
      - Previous chemotherapy or radiation therapy
      - Preexisting neutropenia
      - Cytopenias due to bone marrow involvement by tumor
      - Poor nutritional status
      - Presence of open wounds or active infections
      - Recent surgery
      - Advanced cancer
      - Poor renal function
      - Liver dysfunction, most notably elevated bilirubin
      - Other serious comorbidities
- For secondary prophylaxis of febrile neutropenia:
  - Must be receiving a chemotherapy regimen with a dosing frequency of once every 2 weeks or greater
  - Must be experiencing a neutropenic complication from a prior cycle of chemotherapy for which primary prophylaxis was not received, in which a

reduced dose may compromise disease-free or overall survival or treatment outcome

4. For Sargramostim (Leukine)

- For use in Acute Myeloid Leukemia (AML):
  - Must be age 55 or older
  - Must have a diagnosis of AML and receiving induction chemotherapy therapy
- For use in bone marrow transplant, must have ONE of the following:
  - Must require administration after autologous (not allogeneic) bone marrow transplant for non-Hodgkin's lymphoma (NHL), acute lymphoblastic leukemia (ALL) or Hodgkin's disease
  - Must require mobilization of progenitor cells into peripheral blood, often in conjunction with chemotherapy, for collection by leukapheresis
  - Must have undergone allogeneic bone marrow transplant from HLA
- For use in Hematopoietic Syndrome of Acute Radiation Syndrome [H-ARS]:
  - Must have been exposed to myelosuppressive doses of radiation (suspected or confirmed)

Reauthorization Criteria:

All prior authorization renewals are reviewed 3-month basis to determine the Medical Necessity for continuation of therapy. Authorization may be extended at 3-month intervals based upon chart documentation from the prescriber that the member's condition has improved based upon the prescriber's assessment while on therapy. For H-ARS: must provide documentation that the member's CBC is being closely monitored to determine need for continued treatment.

Limitations:

Length of Authorization (if above criteria met)	
Initial Authorization	Up to 3 months
Reauthorization	Up to 3 months, for 3 months at a time

If the established criteria are not met, the request is referred to a Medical Director for review.

REFERENCES

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4. Leukine [prescribing information]. Bridgewater, NJ; sanofi-aventis U.S. LLC; March 2018
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REVIEW HISTORY

DESCRIPTION OF REVIEW / REVISION	DATE APPROVED
Annual Review	*02/16, 02/17, 02/18*
Preferred Product Update (effective 4/1/18)	*02/18*
New Indication (Leukine)	*05/18*