Geisinger

POLICIES AND PROCEDURE MANUAL

Policy: MBP 59.0

Section: Medical Benefit Pharmaceutical Policy

Subject: White Blood Cell Stimulating Factors

I. Policy:
White Blood Cell Stimulating Factors

II. Purpose/Objective:
To provide a policy of coverage regarding White Blood Cell Stimulating Factors

III. Responsibility:
A. Medical Directors
B. Medical Management
C. Pharmacy Department

IV. Required Definitions
1. Attachment – a supporting document that is developed and maintained by the policy writer or department requiring/authoring the policy.
2. Exhibit – a supporting document developed and maintained in a department other than
3. the department requiring/authoring the policy.
4. Devised – the date the policy was implemented.
5. Revised – the date of every revision to the policy, including typographical and grammatical changes.
6. Reviewed – the date documenting the annual review if the policy has no revisions necessary.

V. Additional Definitions
Medical Necessity or Medically Necessary means Covered Services rendered by a Health Care Provider that the Plan determines are:

a. appropriate for the symptoms and diagnosis or treatment of the Member's condition, illness, disease or injury;
b. provided for the diagnosis and the direct care and treatment of the Member's condition, illness disease or injury;
c. in accordance with current standards good medical treatment practiced by the general medical community;
d. not primarily for the convenience of the Member, or the Member's Health Care Provider; and
e. the most appropriate source or level of service that can safely be provided to the Member. When applied to hospitalization, this further means that the Member requires acute care as an inpatient due to the nature of the services rendered or the Member's condition, and the Member cannot receive safe or adequate care as an outpatient

Medicaid Business Segment
Medically Necessary — A service, item, procedure, or level of care compensable under the Medical Assistance program that is necessary for the proper treatment or management of an illness, injury, or disability is one that:

i. Will, or is reasonably expected to, prevent the onset of an illness, condition, injury or disability.
ii. Will, or is reasonably expected to, reduce or ameliorate the physical, mental or developmental effects of an illness, condition, injury or disability.
iii. Will assist the Member to achieve or maintain maximum functional capacity in performing daily activities, taking into account both the functional capacity of the Member and those functional capacities that are appropriate for Members of the same age.

DESCRIPTION:
White blood cell stimulating factors such as granulocyte colony stimulating factors (G-CSF) [e.g., Neupogen (*filgrastim),* Neulasta (*pegfilgrastim)*, Nivestym (*filgrastim-aafi*), Releuko (*filgrastim-ayow*), Nyvepria (pegfilgrastim-apgf), Fulphila (*pegfilgrastim-jmdb*)*,* Udenyca *(pegfilgrastim-cbqv),* Ziextenzo *(pegfilgrastim-bmez),* Fylnetra *(pegfilgrastim-pbbk)*, Stimufend *(pegfilgrastim-fpgk)*, Rolvedon *(eflapegrastim-xnst)*, Zarxio (*pegfilgrastim-sndz),* and Granix (*tbo-filgrastim)*] and granulocyte-macrophage colony stimulating factor (GM-CSF) [e.g., Leukine (*sargramostim)*] are synthetic stimulants and anti-neutropenic agents administered to decrease the incidence and/or severity of infection associated with drug-related myelosuppression and to assist recovery of hematopoietic function in neutropenia.

CRITERIA FOR USE: Requires Prior Authorization by Medical Director or Designee

Neupogen, Neulasta, Nivestym, Fulphila, Udenyca, Ziextenzo, Zarxio, Leukine, Granix, Releuko, Nyvepria, Fylnetra, Stimufend, and Rolvedon:

The use of a white blood cell stimulating factor [Neupogen (filgrastim), Neulasta (pegfilgrastim), Nivestym (filgrastim-aafi), Fulphila (pegfilgrastim-jmdb), Udenyca *(*pegfilgrastim-cbqv*),* Granix (tbo-filgrastim), Ziextenzo *(*pegfilgrastim-bmez*),* Zarxio (filgrastim-sndz), Releuko (filgrastim-ayow), Nyvepria (pegfilgrastim-apgf), Fylnetra (pegfilgrastim-pbbk), Stimufend (pegfilgrastim-fpgk), Rolvedon (eflapegrastim-xnst), or Leukine (sargramostim)] is considered medically necessary for the commercial, exchange, and CHIP lines of business in insured individuals with a diagnosis of cancer, and when any of the following FDA labeled indications or uses supported by clinical guidelines are present:

1. Primary Prophylaxis - the prevention of febrile neutropenia (FN) when the risk of FN due to the myelosuppressive chemotherapy regimen is 20% or greater. Those regimens include but are not limited to:

- TC (paclitaxel/cisplatin, or cyclophosphamide/docetaxel or docetaxel/cisplatin or paclitaxel/carboplatin)
- MVAC (methotrexate, vinblastine, doxorubicin, cisplatin)
- AC (doxorubicin, cyclophosphamide, docetaxel)
- AT (doxorubicin, paclitaxel)
- TIC (paclitaxel, ifosfamide, mesna, cisplatin)
- VAPEC-B (vincristine, doxorubicin, prednisolone, etoposide, cyclophosphamide, bleomycin)
- DHAP (dexamethasone, cisplatin, cytarabine)

NOTE: *Regimens not specified in this document must be listed on a nationally recognized guideline stating risk of FN of greater than 20%.*

AND

- For requests for Neulasta/Neulasta Onpro, medical record documentation of a therapeutic failure on, intolerance to, or contraindication to Ziextenzo, Udenyca, Nyvepria, Fylnetra, Stimufend, **AND** Fulphila.

OR

For the prevention of FN when the risk of developing FN is less than 20%, but any other risk factor listed below is present:

- Age 65 years or greater
- Poor performance status
- Previous history of FN
- Extensive prior radiation or chemotherapy treatment
- Poor nutritional status
- Recent surgery or Open wounds or active infection
- Advanced cancer
- Persistent neutropenia
- Bone marrow involvement by tumor
- Liver dysfunction (bilirubin >2.0)
- Renal dysfunction (CrCl <50)

AND

- For requests for Neulasta/Neulasta Onpro, medical record documentation of a therapeutic failure on, intolerance to, or contraindication to Ziextenzo, Udenyca, Nyvepria, Fylnetra, Stimufend, **AND** Fulphila.

Neupogen, Neulasta, Nivestym, Fulphila, Udenyca, Releuko, Nyvepria, Ziextenzo, Zarxio, or Leukine: May also be considered medically necessary for any of the following:

2. Secondary Prophylaxis – prevention of FN when a previous cycle of chemotherapy resulted in a neutropenic complication and for which primary prophylaxis was not received, and a dose reduction will compromise disease-free or overall survival or treatment outcome.

AND

- For requests for Neulasta/Neulasta Onpro, medical record documentation of a therapeutic failure on, intolerance to, or contraindication to Ziextenzo, Udenyca, Nyvepria, Fylnetra, Stimufend, **AND** Fulphila.

3. Treatment of Febrile Neutropenia - as an adjunct to antibiotics in high-risk individuals with FN who are at high risk for infection related complications or when **any** of the following prognostic factors are documented:

- Age 65 years or greater
- Anticipated prolonged and profound neutropenia
- Uncontrolled primary disease
- Pneumonia
- Invasive fungal infection
- Hypotension
- Multi-organ dysfunction
- Hospitalized at the time of development of the fever

AND

- For requests for Neulasta/Neulasta Onpro, medical record documentation of a therapeutic failure on, intolerance to, or contraindication to Ziextenzo, Udenyca, Fylnetra, Stimufend, **AND** Fulphila.

4. Dose Dense Therapy – specifically in the treatment of node positive breast cancer, small cell lung cancer, and diffuse aggressive non-Hodgkin's lymphoma.

AND

- For requests for Neulasta/Neulasta Onpro, medical record documentation of a therapeutic failure on, intolerance to, or contraindication to Ziextenzo, Udenyca, Nyvepria, Fylnetra, Stimufend, **AND** Fulphila.

5. Stem Cell Transplantation- when one of the following is met:

- Bone Marrow Transplant (BMT)
  - Documentation of a non-myeloid malignancy undergoing myeloablative chemotherapy followed by autologous or allogenic bone marrow transplant (G-CSF is given after BMT)

OR

- Peripheral Blood Progenitor Cell (Mobilization)Transplant (PBPC)
  - Used for mobilization of autologous hematopoietic progenitor cells into the peripheral blood for collection by leukapheresis. (G-CSF is given prior to and throughout leukapheresis)

AND

- For requests for Neulasta/Neulasta Onpro, medical record documentation of a therapeutic failure on, intolerance to, or contraindication to Ziextenzo, Udenyca, Nyvepria, Fylnetra, Stimufend, **AND** Fulphila.

Note: Neulasta, Udenyca, Ziextenzo, Nyvepria, Fylnetra, Stimufend, and Fulphila are considered off-label for PBPC mobilization. Rolvedon is not indicated for PBPC mobilization.

6. Leukemia or Myelodysplastic Syndromes – insured individuals with any of the following conditions:

- Acute myeloid leukemia (AML) receiving induction or consolidation chemotherapy
- Acute lymphoblastic leukemia (ALL) after completion of the first few days of chemotherapy of the initial induction or the first post-remission course
- Myelodysplastic syndrome with less than 15% blasts in the bone marrow, or recurrent neutropenic infections are experienced.

AND

- For requests for Neulasta/Neulasta Onpro, medical record documentation of a therapeutic failure on, intolerance to, or contraindication to Ziextenzo, Udenyca, Fylnetra, Stimufend, **AND** Fulphila.

7. Lymphoma – Age 65 years or greater treated with curative chemotherapy, e.g., CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone)

AND

- For requests for Neulasta/Neulasta Onpro, medical record documentation of a therapeutic failure on, intolerance to, or contraindication to Ziextenzo, Udenyca, Nyvepria, Fylnetra, Stimufend, **AND** Fulphila.

8. Radiation therapy – with any of the following conditions

- If prolonged delays secondary to neutropenia are anticipated.
- As treatment for radiation injury secondary to doses of 3-10 Grays (Gy) or greater

AND

- For requests for Neulasta/Neulasta Onpro, medical record documentation of a therapeutic failure on, intolerance to, or contraindication to Ziextenzo, Udenyca, Nyvepria, **AND** Fulphila.

Note: Fulphila, Ziextenzo, Fylnetra, Stimufend, and Nyvepria are not indicated for radiation injury syndrome; however, the biosimilars are considered medically accepted for this indication by the NCCN guidelines.

Note: Rolvedon is not indicated for radiation injury syndrome.

Neupogen, Nivestym, Releuko, and Zarxio: May also be considered medically necessary for the following:

9. Severe Chronic Neutropenia – when the following criteria are met
- Diagnosis of Congenital, Cyclic, or Idiopathic Neutropenia AND
- Documentation of an Absolute Neutrophil Count (ANC) <500 cells/mm^3 on three separate occasions during a 6 month period (for Congenital or Idiopathic Neutropenia) OR five consecutive days of ANC <500 cells/mm^3 per cycle (for Cyclic Neutropenia) AND
- Documentation that the member experienced a clinically significant infection, fever, or oropharyngeal ulcer during the past 12 months.

Leukine: May also be considered medically necessary for the following:

10. Delayed Neutrophil Recovery or Graft Failure
- Medical record documentation that the member has had an allogeneic or autologous bone marrow transplant and neutrophil recovery* has not occurred.

  *Note to reviewer: Neutrophil engraftment is defined as the first day of three consecutive days where the neutrophil count (ANC) is 500 cells/mm^3 or greater.

AUTHORIZATION: When approved, the duration of the authorization will be for 6 months.

QUANTITY LIMITS:
- **Ziextenzo**: Facets RX Count: 144 (Q5120 Units), Darwin QL: 0.043mL per day (1 syringe per 14 days)
- **Udenyca**: Facets RX Count: 144 (Q5111 Units), Darwin QL: 0.043mL per day (1 syringe per 14 days)
- **Fulphila**: Facets RX Count: 144 (Q5108 Units), Darwin QL: 0.043mL per day (1 syringe per 14 days)
- **Nyvepria**: Facets RX Count: 144 (Q5122 Units), Darwin QL: 0.043 ML per day (1 syringe per 14 days)
- **Fylnetra**: Facets RX Count: 144 (Q5130 Units), Darwin QL: 0.043 ML per day (1 syringe per 14 days)
- **Stimufend**: Facets RX Count: 144 (Q5127 Units), Darwin QL: 0.043 ML per day (1 syringe per 14 days)
- **Rolvedon**: Facets RX Count: 1584 (J1449 Units), Darwin QL: 0.043 ML per day (1 syringe per 14 days)
- **Neulasta/Neulasta Onpro**: Facets RX Count: 144 (J2506 Units), Darwin QL: 0.043mL per day (1 syringe per 14 days)

EXCLUSIONS: There is insufficient evidence in the published, peer reviewed medical literature to clearly establish that the use of colony stimulating factors (CSF) improves the health outcomes in any of the following indications. The use of CSF's for the following indications is considered not medically necessary and are **NOT COVERED:**
- Routine use as prophylaxis on most chemotherapy regimens; or
- Use as prophylaxis during chemotherapy regimens with a febrile neutropenia risk of less than 20% and no high risk for complications; or
- Use in insured members who are neutropenic but afebrile and not meeting any of the above criteria; or
- Use as an adjunct to antibiotics in uncomplicated febrile neutropenia; or use in relapsed or refractory myeloid leukemia; or
- Use in chemo-sensitization of myeloid leukemias; or
- Use prior to or concurrent with chemotherapy for acute myeloid leukemia; or
- Use prior to or concurrently with chemotherapy for "priming" effect; or
- Use to allow an increase in the dose-intensity of cytotoxic chemotherapy beyond the established dose ranges for these regimens; or
- Use during concomitant chemotherapy and radiation therapy; or
- Continued use if no response is seen within 45 days.

The use of a white blood cell stimulating factor [Neupogen (filgrastim), Neulasta (pegfilgrastim), Nivestym (filgrastim-aafi), Fulphila (pegfilgrastim-jmdb), Udenyca *(*pegfilgrastim-cbqv*),* Granix (tbo-filgrastim), Ziextenzo *(*pegfilgrastim-bmez*),* Zarxio (filgrastim-sndz), Releuko (filgrastim-ayow), Nyvepria (pegfilgrastim-apgf), Fylnetra (pegfilgrastim-pbbk), Stimufend (pegfilgrastim-fpgk), Rolvedon (eflapegrastim-xnst), or Leukine (sargramostim)] is considered medically necessary for the Medicare line of business in insured individuals with a diagnosis of cancer, and when any of the following FDA labeled indications or uses supported by clinical guidelines are present:

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- Use in chemo-sensitization of myeloid leukemias; or
- Use prior to or concurrent with chemotherapy for acute myeloid leukemia; or
- Use prior to or concurrently with chemotherapy for "priming" effect; or
- Use to allow an increase in the dose-intensity of cytotoxic chemotherapy beyond the established dose ranges for these regimens; or
- Use during concomitant chemotherapy and radiation therapy; or
- Continued use if no response is seen within 45 days.

LINE OF BUSINESS:
Eligibility and contract specific benefit limitations and/or exclusions will apply. Coverage statements found in the line of business specific benefit document will supersede this policy.

This policy will be revised as necessary and reviewed no less than annually.

Devised: 12/18/07

Revised: 1/13; 7/14(add drug and auth info), 3/24/15 (formatting), 11/17/15 (added Zarxio), 5/15/18 (chronic neutropenia), 9/18/18 (Leukine), 11/20/18 (Fulphila), 1/15/19 (removed ANCVB), 3/19/19 (Nivestym), 5/21/19 (Udenyca), 7/21/20 (Ziextenzo), 6/8/22 (Neulasta Jcode and Facets count), 7/19/22 (Nyvepria & Releuko), 7/12/23 (LOB carve out, Medicaid business segment), 9/19/23 (Udenyca HSARS [April 2023 P&T], Fylnetra, Stimufend, Rolvedon)

Reviewed: 3/24/15 (formatting), 9/28/16, 7/31/17, 2/1/20, 6/9/21 (formatting)