

Medical Drug Clinical Criteria

Subject:	Colony Stimulating Factor Agents		
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Overview

This document addresses the use of white blood cell growth factors, also known as colony stimulating factors (CSF). There are two types of CSFs, granulocyte and granulocyte-macrophage. Granulocyte colony stimulating factors (G-CSF) are glycoproteins which exert major control over the reproduction and maturation of certain white blood cells. Granulocyte-macrophage colony stimulating factor (GM-CSF) is a hematopoietic growth factor that stimulates proliferation and differentiation of hematopoietic progenitor cells.

The following agents are included in the class

- G-CSF:
 - Granix (tbo-filgrastim)
 - Neulasta Onpro/Neulasta (pegfilgrastim) and Biosimilars
 - Fulphila (pegfilgrastim-jmdb)
 - Fylnetra (pegfilgrastim-pbbk)
 - Nyvepria (pegfilgrastim-apgf)
 - Stimufend (pegfilgrastim-fpgk)
 - Udenyca (pegfilgrastim-cbqv)
 - Ziextenzo (pegfilgrastim-bmez)
 - Neupogen (filgrastim) and Biosimilars
 - Nivestym (filgrastim-aafi)
 - Releuko (filgrastim-ayow)
 - Zarxio (filgrastim-sndz)
 - Rolvedon (eflapegrastim-xnst)
- GM-CSF
 - Leukine (sargramostim)

Rolvedon (eflapegrastim-xnst)

Rolvedon is a new nonbiosimilar long-acting hematopoietic growth factor consisting of a recombinant human granulocyte-colony stimulating factor (rhG-CSF) analog conjugated to a human IgG4Fc fragment. The addition of the Fc fragment extend the drug's half-life, which has been used in other marketed biologics (e.g. etanercept). Rolvedon is indicated to decrease the incidence of infection, as manifested by febrile neutropenia, in adult patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with clinically significant incidence of febrile neutropenia. Rolvedon is not indicated for the mobilization of peripheral blood progenitor cells for hematopoietic stem cell transplantation.

Primary prophylaxis of chemotherapy-induced febrile neutropenia

Neutropenia with fever (febrile neutropenia [FN]) is a serious consequence of myelosuppressive chemotherapy that usually results in hospitalization and the need for intravenous antibiotics (Lyman 2014). FN may result in dose reductions, delays, or even discontinuation of chemotherapy, which, in turn, may compromise patient outcomes. It is important to identify which patients are at high risk for developing FN so that patients can receive optimal chemotherapy while their risk for FN is appropriately managed. There are many factors that need to be evaluated to determine a patient's risk of developing FN, which includes type of chemotherapy regimen, type of cancer being treated, and other patient-specific risk factors.

A review of the literature was performed to gain a comprehensive and updated understanding of FN risk associated with chemotherapy regimens and patient-specific FN risk factors. Studies that have analyzed FN risk factors, often have several limitations, including their retrospective nature and small sample sizes. Our assessment of the following patient risk factors and chemotherapy regimens ([see](#)

[appendix](#) below) is after a review of published literature and guidelines from the American Society of Clinical Oncology (ASCO) and National Comprehensive Cancer Network (NCCN).

The patient risk factors for the development of febrile neutropenia include:

- Age greater than 65 years (Lyman 2014; Aagaard 2018); **OR**
- Poor performance status (Eastern Cooperative Oncology Group 3 or 4) or HIV infection (in particular, those with low CD4 counts ($\leq 450/\mu\text{L}$)) but chemotherapy still indicated (Lyman 2014); **OR**
- Prior radiation therapy (within previous 1 year) (Terbuch 2018) (Fujiwara 2017) (Shigeta 2015); **OR**
- Bone marrow involvement by tumor producing cytopenias (Lyman 2014); **OR**
- Persistent neutropenia (absolute neutrophil count [ANC] less than 1500mm^3) (Lyman 2014); **OR**
- Poor renal function (glomerular filtration rate [GFR] less than $60\text{mL}/\text{min}$) (Lyman 2014; Aagaard 2018); **OR**
- Liver dysfunction (liver function tests at least 2X upper limit of normal or bilirubin $> 2.0\text{ mg}/\text{dL}$) (Lyman 2014; Aagaard 2018); **OR**
- Recent surgery performed as part of cancer management within previous 30 days (not to include a procedure such as port placement, drain placement, IVC filter, etc.) (Lyman 2014; Aagaard 2018); **OR**
- History of active infection within previous 60 days (Lyman 2014; Aagaard 2018); **OR**
- Current open wound and chemotherapy cannot be delayed (Lyman 2014; Aagaard 2018).

Other uses

Use of G-CSF agents in damaged myocardium

The use of G-CSF has been proposed as an adjunct to standard therapies to promote mobilization of stem cells and progenitor cells from the bone marrow into the circulating blood to improve repair of the damaged myocardium. The benefits of G-CSF in other fields, such as oncology, has led to research assessing the potential of G-CSF in repairing myocardial tissue and improving clinical outcomes in those with damaged hearts. To date, the published evidence regarding the safety and efficacy of G-CSF has been lacking.

Consider as additional supportive care for neutropenic patients

The use of G-CSF has been suggested in the NCCN guidelines as a 2A recommendation in supportive care for Grade 1 fever in those using CAR T-cell therapy to prevent progression of cytokine release syndrome (CRS). At this time, there is a lack of published evidence regarding safety and efficacy for this use. A small retrospective analysis in diffuse large B-cell lymphoma members using G-CSF during CAR-T therapy (Gaut 2019) showed no difference in the incidence and severity of infection or incidence of developing CRS between those who received G-CSF and those that did not.

Wilms Tumor (favorable history)

The use of G-CSF has been suggested for use as supportive care in Wilms Tumor (nephroblastoma) after doses of myelosuppressive agents after courses of cyclophosphamide and etoposide and cyclophosphamide, doxorubicin, and vincristine in Regimen M and Regimen I. NCCN currently does not provide any literature support for this use.

Zynteglo (betibeglogene autotemcel) Gene Therapy

Before administration of Zynteglo, hematopoietic stem cells are mobilized with granulocyte colony-stimulating factor and plerixafor, and cells are collected by apheresis. In clinical trials, up to two mobilization cycles (separated by at least 2 weeks) were performed, determined by the need to reach the cumulated target collection number needed for beti-cel manufacture or manufacturing and for rescue cells cryopreserved and stored on site. Prior to apheresis, transfusions are recommended to obtain 8 hemoglobin levels of at least 11 g per deciliter; this hemoglobin level is recommended to be maintained during mobilization and apheresis to suppress stress erythropoiesis.

Definitions and Measures

Absolute neutrophil count (ANC): A measure of the number of neutrophils (a type of white blood cell) in the blood.

Acute Radiation Syndrome (ARS): Also known as radiation sickness.

Adjuvant or adjunctive treatment: Treatment given after the primary treatment to increase the chances of a cure and may include chemotherapy, radiation, hormone or biological therapy.

Febrile neutropenia: Febrile neutropenia can occur as a result of severe neutropenia; defined as the occurrence of fever (greater than or equal to 38.3°C for more than 1 hour) in association with an ANC less than $0.5 \times 10^9/\text{L}$ or ANC less than $1.0 \times 10^9/\text{L}$ and a predicted decline to less than or equal to $0.5 \times 10^9/\text{L}$ over the subsequent 48 hours.

ECOG or Eastern Cooperative Oncology Group Performance Status: A scale and criteria used by doctors and researchers to assess how an individual's disease is progressing, assess how the disease affects the daily living abilities of the individual, and determine appropriate treatment and prognosis. This scale may also be referred to as the WHO (World Health Organization) or Zubrod score which is based on the following scale:

- 0 = Fully active, able to carry on all pre-disease performance without restriction
- 1 = Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, for example, light house work, office work
- 2 = Ambulatory and capable of all self-care but unable to carry out any work activities. Up and about more than 50% of waking hours
- 3 = Capable of only limited self-care, confined to bed or chair more than 50% of waking hours
- 4 = Completely disabled. Cannot carry on any self-care. Totally confined to bed or chair
- 5 = Dead

Neutropenia: A decrease in the number of neutrophils (white blood cells that respond quickly to infection) in the blood. Neutrophils less than $1,500/\text{mm}^3$ is considered to be neutropenic and at risk for infection. Neutrophils fewer than $500\text{ cells}/\text{mm}^3$ is considered at high risk of infection.

Neutrophil: A type of white blood cell that helps fight infection.

Primary prophylaxis: Prevention of febrile neutropenia with the first cycle of a specified chemotherapy regimen.

Secondary prophylaxis: Prevention of febrile neutropenia given with the second and/or subsequent cycle of a given regimen of chemotherapy for individuals who had a neutropenic complication from the preceding cycle of chemotherapy and there is no plan to reduce the dose intensity.

Clinical Criteria

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

Rolvedon (eflapegastim-xnst)

Requests for Rolvedon (eflapegastim-xnst) may be approved if the following criteria are met:

- I. Individual with nonmyeloid malignancy is using for primary prophylaxis of Febrile Neutropenia (FN); **AND**
- II. Individual has a risk of FN of 20% or greater based on chemotherapy regimen (NCCN 2A) ([see Appendix](#), Table 1);

OR

- III. Individual with nonmyeloid malignancy is using for primary prophylaxis of FN; **AND**
- IV. Individual has a risk of developing FN is greater than or equal to 10% and less than 20% based on chemotherapy regimen ([see Appendix](#), Table 1) and individuals have any of the following risk factors for FN:
 - A. Age greater than 65 years (Lyman 2014; Aagaard 2018); **OR**
 - B. Poor performance status (Eastern Cooperative Oncology Group 3 or 4) or HIV infection (in particular, those with low CD4 counts ($\leq 450/\mu\text{L}$)) but chemotherapy still indicated (Lyman 2014); **OR**
 - C. Prior radiation therapy (within previous 1 year) (Terbuch 2018) (Fujiwara 2017) (Shigeta 2015); **OR**
 - D. Bone marrow involvement by tumor producing cytopenias (Lyman 2014); **OR**
 - E. Persistent neutropenia (absolute neutrophil count [ANC] less than 1500mm^3) (Lyman 2014); **OR**
 - F. Poor renal function (glomerular filtration rate [GFR] less than $60\text{mL}/\text{min}$) (Lyman 2014; Aagaard 2018); **OR**
 - G. Liver dysfunction (liver function tests at least 2X upper limit of normal or bilirubin $> 2.0\text{ mg}/\text{dL}$) (Lyman 2014) (Aagaard 2018); **OR**
 - H. Recent surgery performed as part of cancer management within previous 30 days (not to include a procedure such as port placement, drain placement, IVC filter, etc.) (Lyman 2014; Aagaard 2018); **OR**
 - I. History of active infection within previous 60 days (Lyman 2014; Aagaard 2018); **OR**
 - J. Current open wound and chemotherapy cannot be delayed (Lyman 2014; Aagaard 2018).

OR

- V. Individual with nonmyeloid malignancy is using for secondary prophylaxis of FN; **AND**
- VI. Individual has experienced a neutropenic complication from a prior cycle of chemotherapy (for which prophylaxis was not received), in which a reduced dose may compromise disease-free or overall survival or treatment outcome (NCCN 2A);

OR

- VII. Individual is using as adjunctive treatment for FN; **AND**
- VIII. Individual has not received prophylactic therapy with pegfilgrastim (NCCN 2A); **AND**
- IX. Individual has a high risk for infection-associated complications as demonstrated by any of the following:
 - A. Expected prolonged (greater than 10 days) and profound (less than $0.1 \times 10^9/\text{L}$) neutropenia; **OR**
 - B. Age greater than 65 years; **OR**
 - C. Pneumonia or other clinically documented infections; **OR**
 - D. Hypotension and multi organ dysfunction (sepsis syndrome); **OR**
 - E. Invasive fungal infection; **OR**
 - F. Prior episode of febrile neutropenia; **OR**
 - G. Hospitalized at the time of the development of fever.

OR

- X. Individual is using for autologous hematopoietic stem cell (HSC) mobilization as part of the development of an FDA-approved ex vivo gene therapy (e.g. Zynteglo (betibeglogene autotemcel)).

Neulasta/Neulasta Onpro (pegfilgrastim), Fulphila (pegfilgrastim-jmdb), Fylnetra (pegfilgrastim-pbbk), Nyvepria (pegfilgrastim-apgf), Stimufend (pegfilgrastim-fpgk), Udenyca (pegfilgrastim-cbqv), or Ziextenzo (pegfilgrastim-bmez)

Requests for Neulasta (pegfilgrastim), Fulphila (pegfilgrastim-jmdb), Fylnetra (pegfilgrastim-pbbk), Nyvepria (pegfilgrastim-apgf), Udenyca (pegfilgrastim-cbqv), or Ziextenzo (pegfilgrastim-bmez) may be approved if the following criteria are met:

- I. Individual with nonmyeloid malignancy is using for primary prophylaxis of Febrile Neutropenia (FN); **AND**
- II. Individual has a risk of FN of 20% or greater based on chemotherapy regimen ([see Appendix](#), Table 1);

OR

- III. Individual with nonmyeloid malignancy is using for primary prophylaxis of FN; **AND**
- IV. Individual's risk of developing FN is greater than or equal to 10% and less than 20% based on chemotherapy regimen ([see Appendix](#), Table 1) and individual has any of the following risk factors for FN:
 - A. Age greater than 65 years (Lyman 2014; Aagaard 2018); **OR**
 - B. Poor performance status (Eastern Cooperative Oncology Group 3 or 4) or HIV infection (in particular, those with low CD4 counts ($\leq 450/\mu\text{L}$)) but chemotherapy still indicated (Lyman 2014); **OR**
 - C. Prior radiation therapy (within previous 1 year) (Terbuch 2018) (Fujiwara 2017) (Shigeta 2015); **OR**
 - D. Bone marrow involvement by tumor producing cytopenias (Lyman 2014); **OR**
 - E. Persistent neutropenia (absolute neutrophil count [ANC] less than 1500mm^3) (Lyman 2014); **OR**
 - F. Poor renal function (glomerular filtration rate [GFR] less than $60\text{mL}/\text{min}$) (Lyman 2014; Aagaard 2018); **OR**
 - G. Liver dysfunction (liver function tests at least 2X upper limit of normal or bilirubin $> 2.0\text{ mg}/\text{dL}$) (Lyman 2014) (Aagaard 2018); **OR**
 - H. Recent surgery performed as part of cancer management within previous 30 days (not to include a procedure such as port placement, drain placement, IVC filter, etc) (Lyman 2014; Aagaard 2018); **OR**
 - I. History of active infection within previous 60 days (Lyman 2014; Aagaard 2018); **OR**
 - J. Current open wound and chemotherapy cannot be delayed (Lyman 2014; Aagaard 2018);

OR

- V. Individual with nonmyeloid malignancy is using for secondary prophylaxis of FN; **AND**
- VI. Individual has experienced a neutropenic complication from a prior cycle of chemotherapy (for which prophylaxis was not received), in which a reduced dose may compromise disease-free or overall survival or treatment outcome (NCCN 2A);

OR

- VII. Individual is using as adjunctive treatment for FN; **AND**
- VIII. Individual has not received prophylactic therapy with pegfilgrastim (NCCN 2A); **AND**
- IX. Individual has a high risk for infection-associated complications as demonstrated by any of the following:
 - A. Expected prolonged (greater than 10 days) and profound (less than $0.1 \times 10^9/\text{L}$) neutropenia; **OR**
 - B. Age greater than 65 years; **OR**
 - C. Pneumonia or other clinically documented infections; **OR**
 - D. Hypotension and multi organ dysfunction (sepsis syndrome); **OR**
 - E. Invasive fungal infection; **OR**
 - F. Prior episode of febrile neutropenia; **OR**
 - G. Hospitalized at the time of the development of fever;

OR

- X. Individual is receiving dose dense therapy (treatment given more frequently, such as every 2 weeks instead of every 3 weeks) for adjuvant treatment of breast cancer (ASCO Smith 2015);

OR

- XI. Individual is using after accidental or intentional total body radiation of myelosuppressive doses (greater than 2 Grays [Gy]) (such as Hematopoietic Syndrome of Acute Radiation Syndrome);

OR

- XII. Individual is using after a hematopoietic progenitor stem cell transplant (HPCT/HSCT) to promote myeloid reconstitution OR when engraftment is delayed or has failed (NCCN 2A);

OR

- XIII. Individual is using for treatment for hematopoietic cell mobilization for autologous donors in combination with plerixafor (NCCN 2A);

OR

- XIV. Individual is using for Wilms Tumor (Nephroblastoma) (NCCN 2A); **AND**
- XV. Using with Regimen M and Regimen I for one of the following courses:
 - A. Cyclophosphamide and etoposide; **OR**
 - B. Cyclophosphamide, doxorubicin, and vincristine;

OR

- XVI. Individual is using for autologous hematopoietic stem cell (HSC) mobilization as part of the development of an FDA-approved ex vivo gene therapy (e.g. Zynteglo (betibeglogene autoemcel)).

Neupogen (filgrastim), Nivestym (filgrastim-aafi), Releuko (filgrastim-ayow), or Zarxio (filgrastim-sndz)

Requests for Neupogen (filgrastim), Nivestym (filgrastim-aafi), Releuko (filgrastim-ayow), or Zarxio (filgrastim-sndz) may be approved if the following criteria are met:

- I. Individual with nonmyeloid malignancy is using for primary prophylaxis of FN; **AND**
- II. Individual has a risk of FN of 20% or greater based on chemotherapy regimen ([see Appendix](#), Table 1);

OR

- III. Individual with nonmyeloid malignancy is using for primary prophylaxis of FN; **AND**
- IV. Individual's risk of developing FN is greater than or equal to 10% and less than 20% based on chemotherapy regimen ([see Appendix](#), Table 1) and individual has any risk factors for FN:
 - A. Age greater than 65 years (Lyman 2014; Aagaard 2018); **OR**
 - B. Poor performance status (Eastern Cooperative Oncology Group 3 or 4) or HIV infection (in particular, those with low CD4 counts ($\leq 450/\mu\text{L}$) but chemotherapy still indicated (Lyman 2014); **OR**
 - C. Prior radiation therapy (within previous 1 year) (Terbuch 2018) (Fujiwara 2017) (Shigeta 2015); **OR**
 - D. Bone marrow involvement by tumor producing cytopenias (Lyman 2014); **OR**
 - E. Persistent neutropenia (absolute neutrophil count [ANC] less than 1500mm^3) (Lyman 2014); **OR**
 - F. Poor renal function (glomerular filtration rate [GFR] less than $60\text{mL}/\text{min}$) (Lyman 2014) (Aagaard 2018); **OR**
 - G. Liver dysfunction (liver function tests at least 2X upper limit of normal or bilirubin $> 2.0\text{ mg}/\text{dL}$) (Lyman 2014; Aagaard 2018); **OR**
 - H. Recent surgery performed as part of cancer management within previous 30 days (not to include a procedure such as port placement, drain placement, IVC filter, etc) (Lyman 2014; Aagaard 2018); **OR**
 - I. History of active infection within previous 60 days (Lyman 2014; Aagaard 2018); **OR**
 - J. Current open wound and chemotherapy cannot be delayed (Lyman 2014; Aagaard 2018);

OR

- V. Individual with nonmyeloid malignancy is using for secondary prophylaxis of FN; **AND**
- VI. Individual has experienced a neutropenic complication from a prior cycle of chemotherapy (for which prophylaxis was not received), in which a reduced dose may compromise disease-free or overall survival or treatment outcome (NCCN 2A);

OR

- VII. Individual is using as adjunctive treatment for FN (NCCN 2A); **AND**
- VIII. Individual has been on prophylactic therapy with filgrastim;
OR
- IX. Individual has not received prophylactic therapy with a granulocyte colony stimulating factor (NCCN Guidelines Myeloid Growth Factors); **AND**
- X. Individual has a high risk for infection-associated complications as demonstrated by any of the following (NCCN 2A):
 - A. Expected prolonged (greater than 10 days) and profound (less than $0.1 \times 10^9/\text{L}$) neutropenia; **OR**
 - B. Age greater than 65 years; **OR**
 - C. Pneumonia or other clinically documented infections; **OR**
 - D. Hypotension and multi organ dysfunction (sepsis syndrome); **OR**
 - E. Invasive fungal infection; **OR**
 - F. Prior episode of febrile neutropenia; **OR**
 - G. Hospitalized at the time of the development of fever;

OR

- XI. Individual is 18 years of age or older and has a diagnosis of acute myeloid leukemia (AML); **AND**
- XII. Individual is using shortly after the completion of induction or repeat induction chemotherapy, or after the completion of consolidation chemotherapy for AML;

OR

- XIII. Individual has a diagnosis of hairy cell leukemia with severe neutropenia (AHFS, NCCN Guidelines Hairy Cell Leukemia);

OR

- XIV. Individual has a diagnosis of myelodysplastic syndrome (MDS) (NCCN 2A); **AND**
- XV. Individual has severe neutropenia (ANC less than or equal to 500mm^3) or experiencing recurrent or resistant infections;

OR

XVI. Individual is receiving dose dense therapy (treatment given more frequently, such as every 2 weeks instead of every 3 weeks) for adjuvant treatment of breast cancer (ASCO Smith 2015);

OR

XVII. Individual is using for chronic administration to reduce the incidence and duration of sequelae of neutropenia (for example, fever, infections, oropharyngeal ulcers) in symptomatic individuals with congenital neutropenia, cyclic neutropenia, or idiopathic neutropenia;

OR

XVIII. Individual is using for the treatment of (non-chemotherapy) drug-induced neutropenia (AHFS);

OR

XIX. Individual is less than 21 years of age and is diagnosed with glycogen storage disease type 1b; **AND**

XX. Individual is using for the treatment of low neutrophil counts (AHFS);

OR

XXI. Individual is using for the treatment of neutropenia associated with human immunodeficiency virus infection and antiretroviral therapy (AHFS);

OR

XXII. Individual is using after accidental or intentional total body radiation of myelosuppressive doses (greater than 2 Grays [Gy]) (such as Hematopoietic Syndrome of Acute Radiation Syndrome);

OR

XXIII. Individual is using after a hematopoietic progenitor stem cell transplant (HPCT/HSCT) to promote myeloid reconstitution or when engraftment is delayed or has failed (NCCN 2A);

OR

XXIV. Individual is using to mobilize progenitor cells into peripheral blood for collection by leukapheresis, as an adjunct to peripheral blood/hematopoietic stem cell transplantation (PBSCT/PHSCT);

OR

XXV. Individual is using as an alternate or adjunct to donor leukocyte infusions (DLI) in those with leukemic relapse after an allogeneic hematopoietic stem cell transplant (DrugPoints B lia);

OR

XXVI. Individual is using to reduce the duration of neutropenia and neutropenia related clinical sequelae in those with nonmyeloid malignancies undergoing myeloblastic chemotherapy followed by bone marrow transplant (BMT);

OR

XXVII. Individual is using for treatment for hematopoietic cell mobilization for autologous donors in combination with plerixafor (NCCN 2A);

OR

XXVIII. Individual is using for Wilms Tumor (Nephroblastoma) (NCCN 2A); **AND**

XXIX. Using with Regimen M and Regimen I for one of the following courses:

- A. Cyclophosphamide and etoposide; **OR**
- B. Cyclophosphamide, doxorubicin, and vincristine;

OR

XXX. Individual is using for autologous hematopoietic stem cell (HSC) mobilization as part of the development of an FDA-approved ex vivo gene therapy (e.g. Zynteglo (betibeglogene autoemcel)) (NCCN 2A).

Leukine (Sargramostim)

Requests for Leukine (sargramostim) may be approved if the following criteria are met:

- I. Individual is using as adjunctive treatment for FN; **AND**
- II. Individual has not previously received prophylactic granulocyte colony-stimulating factors (NCCN 2A); **AND**
- III. Individual has a high risk for infection-associated complications as demonstrated by any of the following (NCCN 2A):
 - A. Expected prolonged (greater than 10 days) and profound (less than $0.1 \times 10^9/L$) neutropenia; **OR**
 - B. Age greater than 65 years; **OR**
 - C. Pneumonia or other clinically documented infections; **OR**

- D. Hypotension and multi organ dysfunction (sepsis syndrome); **OR**
- E. Invasive fungal infection; **OR**
- F. Prior episode of febrile neutropenia; **OR**
- G. Hospitalized at the time of the development of fever;

OR
 IV. Individual is receiving dose dense therapy (treatment given more frequently, such as every 2 weeks instead of every 3 weeks) for adjuvant treatment of breast cancer (ASCO Smith 2015);

OR
 V. Individual has a diagnosis of acute myeloid leukemia (AML); **AND**
 VI. Individual is 55 years and older; **AND**
 VII. Individual is using shortly after the completion of induction or repeat induction chemotherapy of AML;

OR
 VIII. Individual has a diagnosis of myelodysplastic syndrome (MDS); **AND**
 IX. Individual has severe neutropenia (ANC less than or equal to 500mm³) or experiencing recurrent or resistant infections (NCCN Guidelines Myelodysplastic Syndromes; AHFS);

OR
 X. Individual is 18 years or older; **AND**
 XI. Individual is using for the mobilization of hematopoietic progenitor cells into peripheral blood for collection by leukapheresis and autologous transplantation

OR
 XII. Individual is 2 years of age and older; **AND**
 XIII. Individual is using for the acceleration of myeloid reconstitution following autologous or allogenic bone marrow transplantation or peripheral blood progenitor cell transplantation;

OR
 XIV. Individual is 2 years of age and older; **AND**
 XV. Individual is using for the treatment of delayed neutrophil recovery or graft failure after autologous or allogenic bone marrow transplantation;

OR
 XVI. Individual is using to increase survival in adult and pediatric individuals (from birth to 17 years of age) acutely exposed to myelosuppressive doses of radiation (such as Hematopoietic Syndrome of Acute Radiation Syndrome (H-ARS));

OR
 XVII. Individual is 18 years of age or younger; **AND**
 XVIII. Individual is diagnosed with relapsed/refractory high-risk neuroblastoma; **AND**
 XIX. Individual is using in combination with dinutuximab (Unituxin), 13-cis-retinoic acid (i.e. isotretinoin) and with or without interleukin-2 (IL-2) (i.e. aldesleukin) ; **AND**
 XX. Individual achieved a partial response to first-line multi-agent, multi-modality therapy (i.e. induction combination chemotherapy, or myeloablative consolidation chemotherapy followed by autologous stem cell transplant);

OR
 XXI. Individual is diagnosed with relapsed/refractory high-risk neuroblastoma; **AND**
 XXII. Individual is using in combination with Danyelza (naxitamab-gqgk).

Granix (Tbo-Filgrastim)

Requests for Granix (Tbo-Filgrastim) may be approved if the following criteria are met:

- I. Individual with non-myeloid malignancy is using for primary prophylaxis of Febrile Neutropenia (FN); **AND**
- II. Individual has a risk of FN of 20% or greater based on chemotherapy regimen ([see Appendix](#), Table 1);

OR
 III. Individual with nonmyeloid malignancy is using for primary prophylaxis of FN; **AND**
 IV. Individual's risk of developing FN is greater than or equal to 10% and less than 20% based on chemotherapy regimen ([see Appendix](#), Table 1) and individual has any risk factors for FN:
 A. Age greater than 65 years (Lyman 2014; Aagaard 2018); **OR**

- B. Poor performance status (Eastern Cooperative Oncology Group 3 or 4) or HIV infection (in particular, those with low CD4 counts ($\leq 450/\mu\text{L}$)) but chemotherapy still indicated (Lyman 2014); **OR**
- C. Prior radiation therapy (within previous 1 year) (Terbuch 2018) (Fujiwara 2017) (Shigeta 2015); **OR**
- D. Bone marrow involvement by tumor producing cytopenias (Lyman 2014); **OR**
- E. Persistent neutropenia (absolute neutrophil count [ANC] less than 1500mm^3) (Lyman 2014); **OR**
- F. Poor renal function (glomerular filtration rate [GFR] less than $60\text{mL}/\text{min}$) (Lyman 2014; Aagaard 2018); **OR**
- G. Liver dysfunction (liver function tests at least 2X upper limit of normal or bilirubin $> 2.0\text{ mg}/\text{dL}$) (Lyman 2014; Aagaard 2018); **OR**
- H. Recent surgery performed as part of cancer management within previous 30 days (not to include a procedure such as port placement, drain placement, IVC filter, etc.) (Lyman 2014; Aagaard 2018); **OR**
- I. History of active infection within previous 60 days (Lyman 2014; Aagaard 2018); **OR**
- J. Current open wound and chemotherapy cannot be delayed (Lyman 2014; Aagaard 2018);

OR

- V. Individual with nonmyeloid malignancy is using for secondary prophylaxis of FN; **AND**
- VI. Individual has experienced a neutropenic complication from a prior cycle of chemotherapy (for which prophylaxis was not received), in which a reduced dose may compromise disease-free or overall survival or treatment outcome (NCCN 2A);

OR

- VII. Individual is using as an adjunctive treatment for FN; **AND**
- VIII. Individual was previously using Granix (tbo-filgrastim) prophylactically (NCCN 2A);
- OR**
- IX. Individual has not received prophylactic therapy with a granulocyte colony stimulating factor (NCCN Guidelines Myeloid Growth Factors);
- AND**
- X. Individual has a high risk for infection-associated complications as demonstrated by any of the following:
 - A. Expected prolonged (greater than 10 days) and profound (less than $0.1 \times 10^9/\text{L}$) neutropenia (NCCN 2A); **OR**
 - B. Age greater than 65 years; **OR**
 - C. Pneumonia or other clinically documented infections; **OR**
 - D. Hypotension and multi organ dysfunction (sepsis syndrome); **OR**
 - E. Invasive fungal infection; **OR**
 - F. Prior episode of febrile neutropenia; **OR**
 - G. Hospitalized at the time of the development of fever;

OR

- XI. Individual is using after a hematopoietic progenitor stem cell transplant (HPCT/HSCT) to promote myeloid reconstitution or when engraftment is delayed or has failed (NCCN 2A);

OR

- XII. Individual has a diagnosis of myelodysplastic syndrome (MDS); **AND**
- XIII. Individual has severe neutropenia (ANC less than or equal to 500mm^3) or experiencing recurrent or resistant infections (NCCN 2A);

OR

- XIV. Individual is using to mobilize progenitor cells into peripheral blood for collection by leukapheresis, as an adjunct to peripheral blood/hematopoietic stem cell transplantation (PBSCT/PHSCT) (AHFS);

OR

- XV. Individual is using for treatment for hematopoietic cell mobilization for autologous donors in combination with plerixafor (NCCN 2A);

OR

- XVI. Individual is using for autologous hematopoietic stem cell (HSC) mobilization as part of the development of an FDA-approved ex vivo gene therapy (e.g. Zynteglo (betibeglogene autoemcel)).

Colony Stimulating Factors (filgrastim and their biosimilars, pegfilgrastim and their biosimilars, sargramostim, and tbo-filgrastim) may not be approved for any of the following:

- I. Individual is using as prophylaxis for febrile neutropenia, except when above criteria are met; **OR**
- II. Individual using as treatment for neutropenia in those who are afebrile, except when above criteria are met; **OR**
- III. Individual is using as adjunctive therapy in those with uncomplicated febrile neutropenia, defined as a fever less than 10 days duration, no evidence of pneumonia, cellulitis, abscess, sinusitis, hypotension, multi-organ dysfunction, or invasive fungal infection, and no uncontrolled malignancies; **OR**
- IV. Individual is using for chemosensitization of myeloid leukemias; **OR**

- V. Individual is using for prophylaxis of FN during concomitant chemotherapy and radiation therapy; **OR**
- VI. Individual is continuing use if no response is seen within 28-42 days (individuals who have failed to respond within this time frame are considered non-responders); **OR**
- VII. Individual is using as a technique to increase the numbers of circulating hematopoietic stem cells as treatment of damaged myocardium.

Step Therapy

Note: When a white blood cell growth factor, also known as a colony stimulating factor (CSF) is deemed approvable based on the clinical criteria above, the benefit plan may have additional criteria requiring the use of a preferred¹ agent or agents.

Non-Preferred Long-acting (pegfilgrastim) Colony Stimulating Factor (CSF) Agents Step Therapy

A list of long-acting preferred white blood cell growth factors is available [here](#).

Requests for a non-preferred Long-acting CSF agent may be approved when the following criteria are met:

- I. Individual has had a trial and inadequate response or intolerance to one preferred Long-acting CSF agent.

Non-Preferred Short-acting (filgrastim) Colony Stimulating Factor (CSF) Agents Step Therapy

A list of short-acting preferred white blood cell growth factors is available [here](#).

Requests for a non-preferred Short-acting CSF agent may be approved when the following criteria are met:

- I. Individual has had a trial and inadequate response or intolerance to one preferred Short-acting CSF agent:

OR

- II. The preferred agent is not FDA-approved for the prescribed indication and the requested non-preferred agent is.

¹Preferred, as used herein, refers to agents that were deemed to be clinically comparable to other agents in the same class or disease category but are preferred based upon clinical evidence and cost effectiveness.

Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

CPT

96377 Application of on-body injector (includes cannula insertion) for timed subcutaneous injection [Neulasta OnPro injector]

HCPCS

Q5122 Injection, pegfilgrastim-apgf, biosimilar, (Nyvepria), 0.5 mg
 Q5120 Injection, pegfilgrastim-bmez, biosimilar, (Ziextenzo), 0.5 mg
 J1442 Injection, filgrastim (G-CSF), excludes biosimilars, 1 microgram [Neupogen]
 J1447 Injection, tbo-filgrastim, 1 microgram [Granix]
 J2506 Injection, pegfilgrastim, excludes biosimilar, 0.5 mg
 J2820 Injection, sargramostim (GM-CSF), 50 mcg [Leukine, Prokine]
 Q5101 Injection, filgrastim-sndz, biosimilar, (Zarxio), 1 microgram
 Q5108 Injection, pegfilgrastim-jmdb, biosimilar, (Fulphila), 0.5 mg
 Q5110 Injection, filgrastim-aafi, biosimilar, (Nivestym), 1 microgram
 Q5111 Injection, pegfilgrastim-cbqv, biosimilar, (Udenyca), 0.5 mg
 Q5125 Injection, filgrastim-ayow, biosimilar, (Releuko), 1 microgram [Releuko]

J1449	Injection, eflapegrastim-xnst, 0.1 mg [Rolvedon]
Q5127	Injection, pegfilgrastim-fpgk (10ylnetra10), biosimilar, 0.5 mg [Stimufend]
Q5130	Injection, pegfilgrastim-pbbk (10ylnetra), biosimilar, 0.5 mg [Fylnetra]

ICD-10 Diagnosis

All diagnoses

Document History

Revised: 05/19/2023

Document History:

- 11/01/2023 – Step therapy table updates.
- 09/18/2023 – Step therapy table updates.
- 08/15/2023 – Step therapy table updates.
- 07/05/2023 – Step therapy table updates.
- 05/19/2023 – Annual Review: Add NCCN 2A use in Wilms Tumor for filgrastim and pegfilgrastim. Update Udencya for new autoinjector dosage formulation. Add criteria for use with Mozobil to Neulasta (and biosimilars), Neupogen (and biosimilars), and Granix. Format quantity limit table for all pegfilgrastim CSF agents (Neulasta and biosimilars). Update Appendix table for FN risk for selected chemotherapy regimens. Coding Reviewed: No changes.
- 05/01/2023 – Step therapy table updates.
- 03/27/2023 – Step therapy table updates.
- 01/25/2023 – Step therapy table updates.
- 12/21/2022 – Step therapy table updates.
- 10/24/2022 – Step therapy table updates.
- 09/12/2022 – Select Review: Add newly FDA approved Rolvedon criteria to document for PA, QL, and Non-Preferred LA CSF Step Therapy. Add new pegfilgrastim biosimilar Stimufend to Neupogen criteria, Non-Preferred LA Step therapy, and add a new QL for Stimufend prefilled syringe. Add criteria within G-CSF agents for use before Zynteglo gene therapy. Step therapy table updates. Coding reviewed: Added HCPCS J3490, C9399 for Rolvedon and Stimufend. Effective 10/1/2022 Added HCPCS Q5125 for Releuko. Removed HCPCS C9096 for Releuko. Effective 4/1/2023 Added HCPCS J1449, Q5127, Q5130 for Rolvedon, Stimufend, Fylnetra. Removed HCPCS J3590, J3490, C9399.
- 08/19/2022 – Select Review: Update Neulasta criteria with addition of new biosimilar Fylnetra. Add Fylnetra as a potential preferred agent in the Long-Acting CSF ST. Add QL for Fylnetra. Coding Reviewed: Added HCPCS J3590.
- 07/25/2022 – Step Therapy table updates.
- 05/20/2022 – Annual Review: Update Neupogen criteria with addition of new biosimilar Releuko. Update criteria for use in high-risk pediatric neuroblastoma (with or without IL-2). Coding Reviewed: Added HCPCS C9096.
- 12/20/2021 – Step Therapy table updates.
- 05/21/2021– Annual Review: Update pegfilgrastim criteria, Long-Acting Step therapy to clarify inclusion of Neulasta and Neulasta Onpro. Coding Review: No changes. 1/1/2022 Coding Review: Added HCPCS J2506, Removed HCPCS J2505.
- 02/26/2021 – Step Therapy table updates.
- 12/14/2020– Select Review: Add criteria for Leukine use in combination with Danyelza for relapsed or refractory neuroblastoma. Coding Reviewed Effective 1/1/2021 Added HCPCS Q5122 Removed HCPCS J3590 for Nyvepria. Effective 2/23/21 Added Neulasta Onpro to J2505.
- 11/20/2020– Select Review: Clarify pegfilgrastim products quantity limits. Add additional FN chemotherapy regimens in Appendix. Coding Reviewed: Removed HCPCS S9537.
- 08/21/2020– Select Review: Update Neulasta criteria to add new biosimilar Nyvepria (pegfilgrastim-apgf). Update NP Long-Acting Step therapy with new biosimilar Nyvepria. Add new quantity limit for Nyvepria. Add the term biosimilars to the “may not be approved” criteria. Updated Appendix for Febrile Neutropenia Risk of Selected Chemotherapy Regimens. Coding Reviewed: Added HCPCS J3590 for Nyvepria, All diagnosis pend
- 05/15/2020– Annual Review: Update Neupogen and Neulasta criteria to remove Acute Lymphocytic Leukemia criteria. Administrative update to Granix for risk factor criteria. Coding reviewed: Added HCPCS Q5120 (Effective 7/1/2020), Deleted 6/30/2020- HCPCS C9058, J3590 .
- 03/16/2020– Select Review: Update criteria for patient specific risk factors when using growth factors in the prophylaxis of febrile neutropenia. Administrative updates made for consistency.
- 02/21/2020– Select Review: Update Leukine criteria to include FDA use in combination for pediatric high-risk neuroblastoma. Update Neupogen criteria to include FDA biosimilar Ziextenzo. Add quantity limits for Ziextenzo. Update Long-acting CSF Step therapy with the addition of Ziextenzo as a potential preferred product. Coding Reviewed: Added HCPCS C9399, C9058, J3590 for Ziextenzo
- 11/15/2019– Select Review: Update May not be approved section to add criteria in use of granulocyte-colony stimulating factor agents in the treatment of damaged myocardium. Coding reviewed: No changes

- 08/16/2019 – Annual Review: Maintain low-, intermediate-, moderate-, high- risk ratings for febrile neutropenia with various chemotherapeutic regimens listed in NCCN Myeloid Growth Factors Guideline. Remove Leukine (sargramostim) prophylaxis criteria for use in primary prophylaxis of febrile neutropenia. Coding Reviewed: No changes.
- 03/18/2019 – Select Review: Update Neulasta and Fulphila criteria with the addition of new pegfilgrastim agent Udecyca. Update NP Long-Acting CSF Step Therapy with the inclusion of Udecyca as a potential preferred product. Remove off-label Clinical Pharmacology indications. Coding Reviewed: No changes.
- 12/20/2018 – HCPCS changes; added Q5111.
- 11/09/2018 – Coding review: J3590 for Fulphila deleted, Q5108 for Fulphila added, Q5110 Nivestym added. Kept ICD-10 at all diagnosis. Criteria to guide medical necessity.
- 09/10/2018 – Annual Review: Archive Colony Stimulating Factor NP ST. Replace with 2 new NP ST, one for short acting agents and the other for long-acting agents.
- 08/17/2018 – Annual Review: Update all PAs according to FDA label and off-label compendia -- AHFS, DrugPoints, and NCCN 2A off-label updates. Included biosimilars Nivestym and Fulphila within Overview table of products, the PA policies, and within the NP CSF Step therapy.

Appendix

Febrile Neutropenia Risk of Selected Chemotherapy Regimens

The following table represents selected chemotherapy regimens requiring further examination in their disease setting and the associated risk for development of febrile neutropenia. This is not a comprehensive list, as there are other regimens that are associated with risk for the development of FN. The FN risk of these other regimens will follow the guidance within the NCCN Guidelines Management of Neutropenia. A high-risk chemotherapy regimen is defined as a $\geq 20\%$ probability of developing febrile neutropenia, an intermediate-risk chemotherapy regimen is associated with ≥ 10 to $\leq 20\%$ incidence of developing FN, and a low-risk chemotherapy regimen is associated with $<10\%$ incidence of developing FN.

Table 1

Disease State	Chemotherapy regimen	Risk of developing FN	References
Breast Cancer	Adjuvant TC in an older adult	Intermediate	Do 2015; Jones 2009; Jones 2006; Kosaka 2015; Younis 2012
Breast Cancer (Metastatic)	Fam-trastuzumab deruxtecan-nxki	Low	Modi S et al. 2020; Modi S et al. 2022; Cortes J et al 2022;
Breast cancer (Neoadjuvant)	Pembrolizumab, paclitaxel, and carboplatin	Intermediate	Schmid P, et al. 2022
Breast Cancer (Metastatic)	Pembrolizumab, and chemotherapy	Low	Cortes J, et al 2022; Tolaney SM et al 2021; Tolaney SM et al 2020; Perez-Garcia JM et al 2021; Shah AN et al 2020; de la Cruz-Merino L et al 2022
Breast Cancer	Metastatic Sacituzumab govitecan-hziy	Low	Bardia A et al 2021; Bardia A et al 2019; Rugo HS et al 2022; Kathpalia M et al. 2023
Breast Cancer	Neoadjuvant TCHP (docetaxel, carboplatin, trastuzumab, and pertuzumab)	High	Gilbar 2014; Hurvitz 2018
Breast Cancer (Advanced)	Docetaxel (dosing of less than 75 mg/m ²)	Low	Harvey V 2006; Mauri D 2010; Rivera E 2008; Sparano JA 2008; Tabernero J 2004
Breast Cancer (Advanced)	Docetaxel (dosing of 75 mg/m ²)	Intermediate	Andersson M 2011; Baselga J 2012; Burris HA 1999; Harvey V 2006; Jones SE 2005; Marty M 2005;
Castrate-Resistant Prostate Cancer (CRPC) (Advanced)	Cabazitaxel	Intermediate	De Bono JS. 2010; Eisenberger M 2017; Oudard S 2017

Cervical Cancer (Advanced)	Cisplatin and paclitaxel ± bevacizumab	Intermediate	Angioli R 2015; Lissoni AA 2009; Lorusso D 2014; Monk BJ 2009; Moore DH 2004; Tewari KS 2014, 2017; Yang Z 2016
	Topotecan	Intermediate	Bookman MA 2000; Coronel J 2009; Lorusso D 2011; Muderspach LI 2001;
	Pembrolizumab and platinum-based chemotherapy ± bevacizumab	Low	Colombo N et al. 2021
Gastroesophageal Cancer	Cisplatin and irinotecan	Intermediate	Ajani JA 2002; Enzinger PC 2016; Ilson DH 2004, 2012; Knox JJ 2010; Newman E 2005
	Nivolumab and FOLFOX or XELOX	Low	Janjigian YY et al. 2021
Germ Cell Tumors (Advanced)	Bleomycin, etoposide, and cisplatin	Intermediate	de Wit R 2012; Fizazi K 2014; Garcia del Muro X 2008; Nichols CR 1991
	Etoposide and cisplatin	Intermediate	Arranz A 2001; Horwich A 2000; Motzer RJ 1995
Head and Neck Cancer (Recurrent/Metastatic)	EGFR-inhibitor (cetuximab or panitumumab) and platinum-based chemotherapy	Low	Burtness B 2005; Vermorken JB 2008; Vermorken JB 2013;
	Pembrolizumab plus platinum-based chemotherapy	Low	Burtness B 2019;
Non-Hodgkin Lymphoma	Gemcitabine, dexamethasone, and cisplatin ± rituximab	Intermediate	Baetz T 2003; Crump M 2004, 2014
Non-Small Cell Lung Cancer	Cisplatin and vinorelbine	Intermediate	Douillard JY 2006; Fossella F 2003; Gebbia V 2008; Georgoulas V 2005; Kenmotsu H 2020; Pujol JL 2005; Winton T 2005
Non-Small Cell Lung Cancer (Advanced)	Docetaxel	Intermediate	Abe T 2015; Barlesi F 2018; Camps C 2006; Georgoulas V 2004; Gridelli C 2004; Hanna N 2004; Herbst RS 2010; Karampeazis A 2011; Kudoh S 2006; Okamoto I 2020; Paz-Ares L 2008
Non-Small Cell Lung Cancer (Advanced)	Docetaxel and cisplatin	Low	Abe T 2015; Fossella F 2003; Kubota K 2015; Schiller JH 2002
Non-Small Cell Lung Cancer (Advanced)	Docetaxel and ramucirumab	Intermediate	Garon 2014; Yoh 2016
Non-Small Cell Lung Cancer (Metastatic)	Carboplatin/cisplatin, pemetrexed, and pembrolizumab	Low	Gandhi 2018; Langer 2016; Rodrigues-Pereira 2011; Scagliotti 2008
Non-Small Cell Lung Cancer (Metastatic, non-squamous)	Carboplatin, paclitaxel, and atezolizumab ± bevacizumab	Low	Lilenbaurm 2005; Ohe 2007; Socinski 2018; Williamson 2005

Non-Small Cell Lung Cancer (Metastatic, squamous)	Carboplatin, paclitaxel/nab-paclitaxel, and pembrolizumab	Low	Gadgeel 2018; Lilenbaum 2005; Ohe 2007; Paz-Ares 2018; Williamson 2005
Ovarian Cancer	Carboplatin and paclitaxel	Low	Clamp 2019; Coleman 2017; Katsumata 2009, 2013; Lhomme 2008; Pignata 2014; Sugiyama 2016; Vasey 2004
Ovarian Cancer (Advanced)	Topotecan	Intermediate	Aoki 2011; Gordon 2001, 2004; Gore 2002; McGonigle 2011; Meier 2009; Sehouli J 2008; Spanuth WA 2007; Swisher 1997
Ovarian Cancer (Advanced)	Carboplatin and docetaxel	Intermediate	Vasey 2004; Vorobiof 2003; Wang 2014
Pancreatic Cancer	FOLFIRINOX	Intermediate	Chloreaan 2019; Conroy 2011; Conroy 2005; Hosein 2012; Okusaka 2014; Peddi 2012; Suker 2016; Thibodeau 2018; Tong 2018
Small Cell Lung Cancer (Extensive Stage)	Carboplatin, etoposide, and atezolizumab	Low	Horn 2018; Kosmidis 1994; Socinski 2009
Soft Tissue Sarcoma (Advanced)	Doxorubicin	High	Judson I 2014; Lorigan P 2007; Nielsen OS 1998; Seddon B 2017; Tap WD 2017; Tap WD 2020

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CC-0002 Colony Stimulating Factor Agents

Short Acting Colony Stimulating Factor Agents

Commercial Medical Benefit

Effective Date	Preferred Agents	Non-Preferred Agents
11/01/2022	Zarxio	Granix Neupogen Nivestym Releuko
11/01/2022 CalPERS For members 18 years and older, step therapy criteria for Neupogen applies to new starts only (defined as no use of Neupogen in the last 12 months)	Zarxio Nivestym Releuko	Neupogen Granix

Medicaid Medical Benefit

Effective Date	Preferred Agents	Non-Preferred Agents
03/15/2020: IN	Zarxio	Granix Neupogen Nivestym
02/01/2023: OH 04/01/2023: DC 05/08/2023: GA, KY, MD, NJ, NV, NY, SC, WNY 09/01/2023: MN	Zarxio	Granix Neupogen Nivestym Releuko

Medicare Medical Benefit

Effective Date	Preferred Agents	Non-Preferred Agents
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12/01/2022	Zarxio	Granix Neupogen Nivestym Releuko
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Long Acting Colony Stimulating Factor Agents

Commercial Medical Benefit

Effective Date	Preferred Agents	Non-Preferred Agents
02/01/2023	Neulasta Neulasta OnPro Udenyca	Fulphila Fylnetra Nyvepria Rolvedon Stimufend Ziextenzo
01/01/2022 CalPERS For members 18 years and older, step therapy criteria applies to new starts only (defined as no use of Neulasta in the last 12 months)	Fulphila Nyvepria Udenyca Ziextenzo	Neulasta Neulasta OnPro
2/1/2023 CalPERS For members 18 years and older, step therapy criteria applies to new starts only (defined as no use of Neulasta in the last 12 months)	Fulphila Fylnetra Nyvepria Stimufend Udenyca Ziextenzo	Neulasta Neulasta OnPro Rolvedon

Medicaid Medical Benefit

Effective Date	Preferred Agents	Non-Preferred Agents
03/01/2021: CA, WNY 04/01/2021: IN	Neulasta Neulasta OnPro Udenyca	Fulphila Nyvepria Ziextenzo
02/01/2023: OH 09/01/2023: GA, MN 10/01/2023: MD, NJ, NV, NY, SC, TN, VA, WI 12/01/2023: CA, KY	Neulasta Neulasta OnPro Udenyca	Fulphila Fylnetra Nyvepria Rolvedon Stimufend Ziextenzo

Medicare Medical Benefit

Effective Date	Preferred Agents	Non-Preferred Agents
04/01/2023	Neulasta Neulasta OnPro Udenyca	Fulphila Fylnetra Nyvepria Rolvedon Stimufend Ziextenzo