Reference number(s)
1930-A

Specialty Guideline Management Neupogen and filgrastim biosimilars

Products Referenced by this Document

Drugs that are listed in the following table include both brand and generic and all dosage forms and strengths unless otherwise stated. Over the counter (OTC) products are not included unless otherwise stated.

Brand Name	Generic Name
Neupogen	filgrastim
Granix	tbo-filgrastim
Nivestym	filgrastim-aafi
Nypozi	filgrastim-txid
Releuko	filgrastim-ayow
Zarxio	filgrastim-sndz

Indications

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-approved Indications

Neupogen

Patients with Cancer Receiving Myelosuppressive Chemotherapy

Neupogen is indicated to 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 with fever.

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 patients with acute myeloid leukemia (AML).

Patients with Cancer Undergoing Bone Marrow Transplantation

Neupogen is indicated to 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 marrow transplantation.

Patients Undergoing Autologous Peripheral Blood Progenitor Cell Collection and Therapy

Neupogen is indicated for the mobilization of autologous hematopoietic progenitor cells into the peripheral blood for collection by leukapheresis.

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.

Patients Acutely Exposed to Myelosuppressive Doses of Radiation (Hematopoietic Syndrome of Acute Radiation Syndrome)

Neupogen is indicated to increase survival in patients acutely exposed to myelosuppressive doses of radiation (Hematopoietic Syndrome of Acute Radiation Syndrome).

Nivestym

Patients with Cancer Receiving Myelosuppressive Chemotherapy

Nivestym is indicated to 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 with fever.

Patients With Acute Myeloid Leukemia Receiving Induction or Consolidation Chemotherapy

Nivestym is indicated for reducing the time to neutrophil recovery and the duration of fever, following induction or consolidation chemotherapy treatment of patients with acute myeloid leukemia (AML).

Patients with Cancer Undergoing Bone Marrow Transplantation (BMT)

Nivestym is indicated to 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 bone marrow transplantation.

Patients Undergoing Autologous Peripheral Blood Progenitor Cell Collection and Therapy

Nivestym is indicated for the mobilization of autologous hematopoietic progenitor cells into the peripheral blood for collection by leukapheresis.

Patients With Severe Chronic Neutropenia

Nivestym 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.

Granix

Granix is indicated to reduce the duration of severe neutropenia in adult and pediatric patients 1 month and older with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a clinically significant incidence of febrile neutropenia.

Zarxio

Patients with Cancer Receiving Myelosuppressive Chemotherapy

Zarxio is indicated to 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 with fever.

Patients With Acute Myeloid Leukemia Receiving Induction or Consolidation Chemotherapy

Zarxio is indicated for reducing the time to neutrophil recovery and the duration of fever, following induction or consolidation chemotherapy treatment of patients with acute myeloid leukemia (AML).

Patients with Cancer Undergoing Bone Marrow Transplantation

Zarxio is indicated to 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 bone marrow transplantation.

Patients Undergoing Autologous Peripheral Blood Progenitor Cell Collection and Therapy

Zarxio is indicated for the mobilization of autologous hematopoietic progenitor cells into the peripheral blood for collection by leukapheresis.

Patients With Severe Chronic Neutropenia

Zarxio 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.

Releuko

Patients with Cancer Receiving Myelosuppressive Chemotherapy

Releuko is indicated to 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 with fever.

Patients With Acute Myeloid Leukemia Receiving Induction or Consolidation Chemotherapy

Releuko is indicated for reducing the time to neutrophil recovery and the duration of fever, following induction or consolidation chemotherapy treatment of patients with acute myeloid leukemia (AML).

Patients with Cancer Undergoing Bone Marrow Transplantation

Releuko is indicated to 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 bone marrow transplantation.

Patients With Severe Chronic Neutropenia

Releuko 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.

Nypozi

Patients with Cancer Receiving Myelosuppressive Chemotherapy

Nypozi is indicated to 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 with fever.

Patients With Acute Myeloid Leukemia Receiving Induction or Consolidation Chemotherapy

Nypozi is indicated for reducing the time to neutrophil recovery and the duration of fever, following induction or consolidation chemotherapy treatment of patients with acute myeloid leukemia (AML).

Patients with Cancer Undergoing Bone Marrow Transplantation

Nypozi is indicated to 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 marrow transplantation.

Patients Undergoing Autologous Peripheral Blood Progenitor Cell Collection and Therapy

Nypozi is indicated for the mobilization of autologous hematopoietic progenitor cells into the peripheral blood for collection by leukapheresis.

Patients With Severe Chronic Neutropenia

Nypozi 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.

Patients Acutely Exposed to Myelosuppressive Doses of Radiation (Hematopoietic Syndrome of Acute Radiation Syndrome)

Nypozi is indicated to increase survival in patients acutely exposed to myelosuppressive doses of radiation.

Compendial Uses

- Treatment of chemotherapy-induced febrile neutropenia
- Prophylaxis for chemotherapy-induced febrile neutropenia in patients with solid tumors
- Treatment of anemia and neutropenia in patients with myelodysplastic syndromes (MDS)

- Stem cell transplantation-related indications
- Agranulocytosis (non-chemotherapy drug induced)
- Aplastic anemia
- Neutropenia related to HIV/AIDS
- Neutropenia related to renal transplantation
- Acute myeloid leukemia
- Supportive care for neutropenic patients with CAR T-cell-related toxicities
- Hairy Cell Leukemia, neutropenic fever
- Chronic Myeloid Leukemia, treatment of persistent neutropenia due to tyrosine kinase inhibitor therapy
- Glycogen Storage Disease (GSD) Type 1

All other indications are considered experimental/investigational and not medically necessary.

Documentation

Primary Prophylaxis of Febrile Neutropenia

- Documentation must be provided of the member's diagnosis and chemotherapeutic regimen.
- If chemotherapeutic regimen has a low or intermediate risk of febrile neutropenia (less than 20%), documentation must be provided outlining the member's risk factors that confirm the member is at high risk for febrile neutropenia.

Coverage Criteria

Neutropenia in cancer patients receiving myelosuppressive chemotherapy

Authorization of 6 months may be granted for prevention or treatment of febrile neutropenia when all of the following criteria are met :

- The requested medication will not be used in combination with other colony stimulating factors within any chemotherapy cycle.
- The member will not receive chemotherapy at the same time as they receive radiation therapy.
- One of the following criteria is met :
    - The requested medication will be used for primary prophylaxis in members with solid tumors or non-myeloid malignancies who have received, are currently receiving, or will be receiving any of the following:

    - Myelosuppressive anti-cancer therapy that is expected to result in 20% or higher incidence of FN (febrile neutropenia) (FN) (*See Appendix A*)
    - Myelosuppressive anti-cancer therapy that is expected to result in 10 – 19% risk of FN (*See Appendix B*) and who are considered to be at high risk of FN because of bone marrow compromise or co-morbidities, or other patient specific risk factors (*See Appendix C*).
    - Myelosuppressive anti-cancer therapy that is expected to result in less than 10% risk of FN and who have at least 2 patient-related risk factors (*See Appendix C*).
- The requested medication will be used for secondary prophylaxis in members with solid tumors or non-myeloid malignancies who experienced a febrile neutropenic complication or a dose-limiting neutropenic event (a nadir or day of treatment count impacting the planned dose of chemotherapy) from a prior cycle of similar chemotherapy, with the same dose and schedule planned for the current cycle (for which primary prophylaxis was not received)
- The requested medication will be used for treatment of high risk FN in members who have any of the following prognostic factors that are predictive of clinical deterioration:
    - Age greater than 65 years
    - Being hospitalized at the time of the development of fever
    - Sepsis syndrome
    - Invasive fungal infection
    - Pneumonia or other clinically documented infection
    - Prolonged (neutropenia expected to last greater than 10 days) or profound (absolute neutrophil count less than 1 x 10^9/L) neutropenia
    - Prior episodes of febrile neutropenia

Other indications

Authorization of 6 months may be granted for members with any of the following indications:

- Myelodysplastic syndrome (anemia or neutropenia)
- Stem cell transplantation-related indications (including applicable gene therapy protocols)
- Agranulocytosis (non-chemotherapy drug induced)
- Aplastic anemia
- Neutropenia related to HIV/AIDS
- Neutropenia related to renal transplantation
- Acute myeloid leukemia
- Severe chronic neutropenia (congenital, cyclic, or idiopathic)
- Hematopoietic Syndrome of Acute Radiation Syndrome
  Treatment for radiation-induced myelosuppression following a radiological/nuclear incident
- CAR T-cell-related toxicities
  Supportive care for neutropenic patients with CAR T-cell-related toxicities
- Hairy Cell Leukemia
  Members with hairy cell leukemia with neutropenic fever following chemotherapy

- Chronic Myeloid Leukemia
  Members with chronic myeloid leukemia (CML) for treatment of persistent neutropenia due to tyrosine kinase inhibitor therapy
- Glycogen Storage Disease (GSD) Type 1
  Individuals with GSD Type 1 for treatment of low neutrophil counts

Continuation of Therapy

All members (including new members) requesting authorization for continuation of therapy must meet all requirements in the coverage criteria.

Appendix

APPENDIX A: Selected Chemotherapy Regimens with an Incidence of Febrile Neutropenia of 20% or Higher†

Acute Lymphoblastic Leukemia:

Select ALL regimens as directed by treatment protocol (see NCCN guidelines ALL)

Bladder Cancer:

Dose dense MVAC (methotrexate, vinblastine, doxorubicin, cisplatin)

Bone Cancer

- VAIA (vincristine, doxorubicin, ifosfamide, and dactinomycin)
- VDC-IE (vincristine, doxorubicin or dactinomycin, and cyclophosphamide alternating with ifosfamide and etoposide)
- Cisplatin/doxorubicin
- VDC (cyclophosphamide, vincristine, doxorubicin or dactinomycin)
- VIDE (vincristine, ifosfamide, doxorubicin or dactinomycin, etoposide)

Breast Cancer:

- Dose-dense AC (doxorubicin, cyclophosphamide) followed by dose-dense paclitaxel
- TAC (docetaxel, doxorubicin, cyclophosphamide)
- TC (docetaxel, cyclophosphamide)
- TCH (docetaxel, carboplatin, trastuzumab)

Head and Neck Squamous Cell Carcinoma

TPF (docetaxel, cisplatin, 5-fluorouracil)

Hodgkin Lymphoma:

- Brentuximab vedotin + AVD (doxorubicin, vinblastine, dacarbazine)
- Escalated BEACOPP (bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, prednisone)

Kidney Cancer:

Doxorubicin/gemcitabine

Non-Hodgkin's Lymphoma:

- CHP (cyclophosphamide, doxorubicin, prednisone) + brentuximab vedotin
- Dose-adjusted EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin) ± rituximab
- ICE (ifosfamide, carboplatin, etoposide) ± rituximab
- Dose-dense CHOP-14 (cyclophosphamide, doxorubicin, vincristine, prednisone) ± rituximab
- MINE (mesna, ifosfamide, mitoxantrone, etoposide) ± rituximab
- DHAP (dexamethasone, cisplatin, cytarabine) ± rituximab
- ESHAP (etoposide, methylprednisolone, cisplatin, cytarabine) ± rituximab
- HyperCVAD ± rituximab (cyclophosphamide, vincristine, doxorubicin, dexamethasone ± rituximab)
- Pola-R-CHP (polatuzumab vedotin-piiq, rituximab, cyclophosphamide, doxorubicin, prednisone)

Melanoma:

Dacarbazine-based combination with IL-2, interferon alpha (dacarbazine, cisplatin, vinblastine, IL-2, interferon alfa)

Multiple Myeloma:

- VTD-PACE (dexamethasone/thalidomide/cisplatin/doxorubicin/cyclophosphamide/etoposide + bortezomib)
- DT-PACE (dexamethasone/thalidomide/cisplatin/doxorubicin/cyclophosphamide/etoposide)

Ovarian Cancer:

- Topotecan ± bevacizumab
- Docetaxel

Soft Tissue Sarcoma:

- MAID (mesna, doxorubicin, ifosfamide, dacarbazine)
- Doxorubicin
- Ifosfamide/doxorubicin

Small Cell Lung Cancer:

Topotecan

Testicular Cancer:

- VelP (vinblastine, ifosfamide, cisplatin)
- VIP (etoposide, ifosfamide, cisplatin)
- TIP (paclitaxel, ifosfamide, cisplatin)

Gestational Trophoblastic Neoplasia:

- EMA/CO (etoposide, methotrexate, dactinomycin/cyclophosphamide, vincristine)
- EMA/EP (etoposide, methotrexate, dactinomycin/etoposide, cisplatin)
- EP/EMA (etoposide, cisplatin/etoposide, methotrexate, dactinomycin)
- TP/TE (paclitaxel, cisplatin/paclitaxel, etoposide)
- BEP (bleomycin, etoposide, cisplatin)
- VIP (etoposide, ifosfamide, cisplatin)
- ICE (ifosfamide, carboplatin, etoposide)

Wilms Tumor:

- Regimen M (vincristine, dactinomycin, doxorubicin, cyclophosphamide, etoposide)
- Regimen I (vincristine, doxorubicin, cyclophosphamide, etoposide)

Applies to chemotherapy regimens with or without monoclonal antibodies (e.g., trastuzumab, rituximab)

† This list is not comprehensive; there are other agents/regimens that have an intermediate/high risk for development of febrile neutropenia.

APPENDIX B: Selected Chemotherapy Regimens with an Incidence of Febrile Neutropenia of 10% to 19%†

Occult Primary – Adenocarcinoma:

Gemcitabine/docetaxel

Breast Cancer:

- Docetaxel ± trastuzumab
- AC (doxorubicin, cyclophosphamide) + sequential docetaxel (taxane portion only)
- AC + sequential docetaxel + trastuzumab
- Paclitaxel every 21 days ± trastuzumab
- TC (docetaxel, cyclophosphamide)

Cervical Cancer:

- Irinotecan
- Cisplatin/topotecan
- Paclitaxel/cisplatin ± bevacizumab
- Topotecan

Colorectal Cancer:

FOLFIRINOX (fluorouracil, leucovorin, oxaliplatin, irinotecan)

Esophageal and Gastric Cancers:

Irinotecan/cisplatin

Non-Hodgkin's Lymphomas:

- GDP (gemcitabine, dexamethasone, cisplatin/carboplatin)
- GDP (gemcitabine, dexamethasone, cisplatin/carboplatin) + rituximab
- CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) including regimens with pegylated liposomal doxorubicin
- CHOP + rituximab (cyclophosphamide, doxorubicin, vincristine, prednisone, rituximab) including regimens with pegylated liposomal doxorubicin
- Bendamustine

Non-Small Cell Lung Cancer:

- Cisplatin/paclitaxel
- Cisplatin/vinorelbine
- Cisplatin/docetaxel
- Cisplatin/etoposide
- Carboplatin/paclitaxel
- Docetaxel

Ovarian Cancer:

Carboplatin/docetaxel

Pancreatic Cancer:

FOLFIRINOX (fluorouracil, leucovorin, oxaliplatin, irinotecan)

Prostate Cancer:

Cabazitaxel

Small Cell Lung Cancer:

Etoposide/carboplatin

Testicular Cancer:

- BEP (bleomycin, etoposide, cisplatin)
- Etoposide/cisplatin

Uterine Sarcoma:

Docetaxel

Applies to chemotherapy regimens with or without monoclonal antibodies (e.g., trastuzumab, rituximab)

† This list is not comprehensive; there are other agents/regimens that have an intermediate/high risk for development of febrile neutropenia.

APPENDIX C: Patient Risk Factors

- Active infections, open wounds, or recent surgery
- Age greater than or equal to 65 years
- Bone marrow involvement by tumor producing cytopenias
- Previous chemotherapy or radiation therapy
- Poor nutritional status
- Poor performance status
- Previous episodes of FN
- Other serious co-morbidities, including renal dysfunction, liver dysfunction, HIV infection, cardiovascular disease
- Persistent neutropenia

This list is not all-inclusive.

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