

Specialty Guideline Management

Leukine

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
Leukine	sargramostim

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 Indications¹

Acute Myeloid Leukemia Following Induction Chemotherapy

Leukine is indicated to shorten time to neutrophil recovery and to reduce the incidence of severe, life-threatening, or fatal infections following induction chemotherapy in adult patients 55 years and older with acute myeloid leukemia (AML).

Autologous Peripheral Blood Progenitor Cells Mobilization and Collection

Leukine is indicated in adult patients with cancer undergoing autologous hematopoietic stem cell transplantation for the mobilization of hematopoietic progenitor cells into peripheral blood for collection by leukapheresis.

Autologous Peripheral Blood Progenitor Cell and Bone Marrow Transplantation

Leukine is indicated for acceleration of myeloid reconstitution following autologous peripheral blood progenitor cell (PBPC) or bone marrow transplantation in adult and pediatric patients 2 years of age and

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older with non-Hodgkin's lymphoma (NHL), acute lymphoblastic leukemia (ALL) and Hodgkin's lymphoma (HL).

Allogeneic Bone Marrow Transplantation (BMT)

Leukine is indicated for the acceleration of myeloid reconstitution in adult and pediatric patients 2 years of age and older undergoing allogeneic BMT from human leukocyte antigens (HLA)-matched related donors.

Allogenic or Autologous Bone Marrow Transplantation: Treatment of Delayed Neutrophil Recovery or Graft Failure

Leukine is indicated for the treatment of adult and pediatric patients 2 years and older who have undergone allogeneic or autologous BMT in whom neutrophil recovery is delayed or failed.

Acute Exposure to Myelosuppressive Doses of Radiation (H-ARS)

Leukine is indicated 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]).

Compendial Uses²⁻¹⁰

- Prophylaxis and treatment of chemotherapy-induced febrile neutropenia in non-myeloid malignancies
- Treatment of neutropenia and anemia in patients with myelodysplastic syndromes (MDS)
- Acute myeloid leukemia
- Agranulocytosis (non-chemotherapy drug induced)
- Aplastic anemia
- Neutropenia related to HIV/AIDS
- Stem cell transplantation-related indications
- Neuroblastoma
- Severe chronic neutropenia (congenital, cyclic, or idiopathic)

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 (20% and less), 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 chemotherapy¹⁻⁸

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 greater than 20% incidence of febrile neutropenia (FN) (See Appendix A).
 - Myelosuppressive anti-cancer therapy that is expected to result in 10 – 20% risk of FN (See Appendix B) and who are considered to be at high risk of FN because of bone marrow compromise, comorbidities, 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 febrile neutropenia (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 $0.1 \times 10^9/L$) neutropenia
 - Prior episodes of febrile neutropenia

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Neuroblastoma²

Authorization of 6 months may be granted for treatment of high-risk neuroblastoma when used with one of the following:

- Dinutuximab (Unituxin) and isotretinoin (13-cis-retinoic acid [RA])
- Temozolomide, irinotecan, and dinutuximab (Unituxin)
- Temozolomide, irinotecan, and naxitamab-gqqk (Danyelza)

Other indications²⁻¹⁰

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

- Myelodysplastic syndrome (anemia or neutropenia)
- Acute myeloid leukemia
- Agranulocytosis (non-chemotherapy drug induced)
- Aplastic anemia
- Neutropenia related to HIV/AIDS
- Stem cell transplantation-related indications
- Severe chronic neutropenia (congenital, cyclic, or idiopathic)
- Hematopoietic Syndrome of Acute Radiation Syndrome: Treatment for radiation-induced myelosuppression following a radiological/nuclear incident

Continuation of Therapy

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

Appendix^{6,8}

Appendix A: Selected Chemotherapy Regimens with an Incidence of Febrile Neutropenia Greater than 20%

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

Acute Lymphoblastic Leukemia:

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

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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)
- Nivolumab + AVD (doxorubicin, vinblastine, dacarbazine)
- Escalated BEACOPP (bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, prednisone)
- BrECADD (brentuximab vedotin, etoposide, cyclophosphamide, doxorubicin, dacarbazine, dexamethasone)

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
- CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone)
- MINE (mesna, ifosfamide, mitoxantrone, etoposide) ± rituximab
- DHAP (dexamethasone, cisplatin, cytarabine) ± rituximab
- ESHAP (etoposide, methylprednisolone, cisplatin, cytarabine (Ara-C)) ± rituximab
- HyperCVAD ± rituximab (cyclophosphamide, vincristine, doxorubicin, dexamethasone ± rituximab)

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- 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
- Carboplatin/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/EP (etoposide, methotrexate, dactinomycin/etoposide, cisplatin)
- EP/EMA (etoposide, cisplatin/etoposide, methotrexate, dactinomycin)
- TP/TE (paclitaxel, cisplatin/paclitaxel, etoposide)
- BEP (bleomycin, etoposide, cisplatin)
- TIP (Paclitaxel, ifosfamide, cisplatin)
- VIP (etoposide, ifosfamide, cisplatin)
- ICE (ifosfamide, carboplatin, etoposide)

Wilms Tumor:

- Regimen M (vincristine, dactinomycin, doxorubicin, cyclophosphamide, etoposide)
- Regimen I (vincristine, doxorubicin, cyclophosphamide, etoposide)
- Revised Regimen UH-1 (vincristine, doxorubicin, cyclophosphamide, carboplatin, etoposide)

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- Revised Regimen UH-2 (vincristine, doxorubicin, cyclophosphamide, carboplatin, etoposide, irinotecan)

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

Appendix B: Selected Chemotherapy Regimens with an Incidence of Febrile Neutropenia of 10% to 20%

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

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
- Sacituzumab govitecan-hziy
- 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

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Non-Small Cell Lung Cancer:

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

Appendix C: Patient Risk Factors

This list is not all-inclusive.

- 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

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