Draft Revised Policy: Do Not Implement

Sargramostim (Leukine®)

IMPORTANT REMINDER

We develop Medical Policies to provide guidance to Members and Providers. This Medical Policy relates only to the services or supplies described in it. The existence of a Medical Policy is not an authorization, certification, explanation of benefits or a contract for the service (or supply) that is referenced in the Medical Policy. For a determination of the benefits that a Member is entitled to receive under his or her health plan, the Member's health plan must be reviewed. If there is a conflict between the medical policy and a health plan or government program (e.g., TennCare), the express terms of the health plan or government program will govern.

The proposal is to add text/statements in red and to delete text/statements with strikethrough:

POLICY

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

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 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 Uses

- 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 (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 ~~FOR INITIAL APPROVAL~~

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 ~~(1, 2, and 3)~~:

- 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 they receive radiation therapy.
- One of the following criteria is met ~~(i, ii, or iii)~~ :
  - 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 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, 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 x 109/L) neutropenia
- Prior episodes of febrile neutropenia

Neuroblastoma

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

- Dinutuximab (Unituxin) ~~interleukin-2 (aldesleukin [Proleukin]),~~ and isotretinoin (13-cis-retinoic acid [RA])
- Temozolomide, irinotecan, and dinutuximab (Unituxin)
- Naxitamab-gqgk (Danyelza)

Other indications

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 ~~initial authorization~~ criteria.

APPENDIX

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

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)

Bladder Cancer:
Dose dense MVAC (methotrexate, vinblastine, doxorubicin, cisplatin)
~~CBDCa/Pac (carboplatin, paclitaxel)~~

Bone Cancer:

- ~~VAI(vincristine, doxorubicin or dactinomycin, ifosfamide)~~
- 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:
~~Docetaxel + trastuzumab~~
- Dose-dense AC (doxorubicin, cyclophosphamide) followed by dose dense paclitaxel ~~(or dose dense paclitaxel)~~
- TAC (docetaxel, doxorubicin, cyclophosphamide)

~~AT (doxorubicin, docetaxel)~~
~~Doc (docetaxel)~~
- TC (docetaxel, cyclophosphamide)
- TCH (docetaxel, carboplatin, trastuzumab)

~~**Colorectal Cancer:**~~
~~FOLFOXIRI (fluorouracil, leucovorin, oxaliplatin, irinotecan)~~
~~**Esophageal and Gastric Cancers:**~~
~~Docetaxel/cisplatin/fluorouracil~~

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 (Ara-C)) ± rituximab
- HyperCVAD ± rituximab (cyclophosphamide, vincristine, doxorubicin, dexamethasone ± rituximab)
- ~~VAPEC-B (vincristine, doxorubicin, prednisolone, etoposide, cyclophosphamide, bleomycin)~~
- 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:
~~Top (~~ Topotecan~~)~~
~~CAV (cyclophosphamide, doxorubicin, vincristine)~~

Testicular Cancer:
- VeIP (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%~~*†~~

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

~~CMF classic (cyclophosphamide, methotrexate, fluorouracil)~~
~~CA (doxorubicin, cyclophosphamide) (60 mg/m2) (hospitalized)~~
- AC (doxorubicin, cyclophosphamide) + sequential docetaxel (taxane portion only)
- AC + sequential docetaxel + trastuzumab

~~A (doxorubicin) (75 mg/m2)~~
~~AC (doxorubicin, cyclophosphamide)~~
~~CapDoc (capecitabine, docetaxel)~~

- Paclitaxel every 21 days ± trastuzumab
- TC (docetaxel, cyclophosphamide)

Cervical Cancer:
- Irinotecan
- Cisplatin/topotecan
- Paclitaxel/cisplatin ± bevacizumab
- Topotecan

Colorectal Cancer:
~~FL (fluorouracil, leucovorin)~~
~~CPT-11 (irinotecan) (350 mg/m2 q 3 wk)~~
~~FOLFOX (fluorouracil, leucovorin, oxaliplatin)~~
FOLFIRINOX (fluorouracil, leucovorin, oxaliplatin, irinotecan)

Esophageal and Gastric Cancers:
Irinotecan/cisplatin
~~Epirubicin/cisplatin/5-fluorouracil~~
~~Epirubicin/cisplatin/capecitabine~~

Non-Hodgkin's Lymphomas:
~~EPOCH-IT chemotherapy~~
- GDP (gemcitabine, dexamethasone, cisplatin/carboplatin)
- GDP (gemcitabine, dexamethasone, cisplatin/carboplatin) + rituximab

~~FMR (fludarabine, mitoxantrone, 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*

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

APPLICABLE TENNESSEE STATE MANDATE REQUIREMENTS

BlueCross BlueShield of Tennessee's Medical Policy complies with Tennessee Code Annotated Section 56-7-2352 regarding coverage of off-label indications of Food and Drug Administration (FDA) approved drugs when the off-label use is recognized in one of the statutorily recognized standard reference compendia or in the published peer-reviewed medical literature.

ADDITIONAL INFORMATION

For appropriate chemotherapy regimens, dosage information, contraindications, precautions, warnings, and monitoring information, please refer to one of the standard reference compendia (e.g., the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) published by the National Comprehensive Cancer Network®, Drugdex Evaluations of Micromedex Solutions at Truven Health, or The American Hospital Formulary Service Drug Information).

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EFFECTIVE DATE

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