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Policy Number: C2439-A

Leukine (sargramostim)

PRODUCTS AFFECTED

Leukine (sargramostim)

COVERAGE POLICY

Coverage for services, procedures, medical devices, and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any. This Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines.

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational, or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

DIAGNOSIS:
Prophylaxis of febrile neutropenia in non-myeloid malignancies following myelosuppressive chemotherapy, Febrile neutropenia prophylaxis in acute myeloid leukemia (AML), Febrile neutropenia prophylaxis following hematopoietic stem cell transplant (HSCT), Peripheral blood progenitor cell collection, Zidovudine-induced neutropenia, Ganciclovir-induced neutropenia, Neuroblastoma, Acute radiation syndrome

REQUIRED MEDICAL INFORMATION:
This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case-by case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review. When the requested drug product for coverage is dosed by weight, body surface area or other member specific measurement, this data element is required as part of the medical necessity review. The Pharmacy and Therapeutics Committee has determined that the drug benefit shall be a mandatory generic and that generic drugs will be dispensed whenever available.

BIOSIMILAR DRUGS are preferred when requested as a physician administered drug and/or pharmacy

PDL/formulary product per applicable state regulations and there is a lack of data demonstrating clinical superiority of reference drugs over the FDA approved biosimilar drugs. A reference medication is approved under the following conditions:

1. Treatment with at least two associated biosimilar drug(s) has been ineffective, resulted in serious side effects, or is contraindicated (i.e., an allergic reaction to a specific inactive ingredient in the preferred biologic productor biosimilar OR an adverse reaction to a specific inactive ingredient in the preferred biologic product or biosimilar OR therapeutic success while taking a non-preferred biologic product or biosimilar and therapeutic failure while taking the preferred biologic product or biosimilar documented by patient diary or medical charted notes)
   [DOCUMENTATION REQUIRED: Document when the preferred biologic product or biosimilar was tried and the length of the trial period. Provide specific clinical documentation of therapeutic failure on the preferred biologic product or biosimilar whenever possible. Describe the medical problem caused by the preferred referenced biologic. Vague and non-descriptive symptoms are not adequate rationale (e.g., stomachache).]

A. FEBRILE NEUTROPENIA PROPHYLAXIS IN NON-MYELOID MALIGNANCIES:

1. Documented diagnosis of non-myeloid malignancy
   AND
2. Documentation that sargramostim is being used following myelosuppressive chemotherapy [DOCUMENTATION REQUIRED of current chemotherapy regimen, any previous chemotherapy regimens and anticipated treatment plan]
   AND
3. (a) Member has a risk of febrile neutropenia (FN) of greater than 20% based on current chemotherapy regimen (as listed in current ASCO and NCCN guidelines for myeloid growth factors [See Appendix])
   OR
   (b) Member has a risk of febrile neutropenia of 10-20% based on chemotherapy regimen, and at least ONE of the following risk factors apply:
   - (i) Prior chemotherapy or radiation therapy
   - (ii) Persistent neutropenia (defined as neutrophil count less than 500 neutrophils/mcL or less than 1,000 neutrophils/mcL and a predicted decline to less than or equal to 500 neutrophils/mcL over next 48 hours)
   - (iii) Bone marrow involvement by tumor
   - (iv) Recent surgery and/or open wounds
   - (v) Liver dysfunction (bilirubin greater than 2.0 mg/dL)
   - (vi) Renal dysfunction (creatinine clearance less than 50 mL/min)
   - (vii) Age greater than 65 receiving full chemotherapy dose intensity

   OR
   (c) Previous neutropenic fever complication from a prior cycle of similar chemotherapy
   OR
   (d) The member is receiving a dose-dense chemotherapy regimen

B. FEBRILE NEUTROPENIA PROPHYLAXIS IN ACUTE MYELOID LEUKEMIA (AML):

1. Documented diagnosis of Acute Myeloid Leukemia (AML)
   AND
2. Documentation that member is receiving either induction chemotherapy OR consolidation chemotherapy [DOCUMENTATION REQUIRED]

C. FEBRILE NEUTROPENIA PROPHYLAXIS FOLLOWING HEMATOPOIETIC STEM CELL TRANSPLANT(HSCT):

1. Documented diagnosis of non-myeloid malignancy
   AND
2. Documentation member is undergoing or must have had a hematopoietic stem cell transplant (HSCT) (e.g., bone marrow transplant, peripheral-blood progenitor cell (PBPC) transplant) for a

non-myeloid malignancy [DOCUMENTATION REQUIRED]

D. TREATMENT OF DELAYED NEUTROPHIL RECOVERY OR GRAFT FAILURE:
   1. Documentation that member underwent allogeneic or autologous bone marrow transplant
      AND
   2. (a) Documentation that member has delay in neutrophil recovery by day 28 post transplant
      OR
      (b) Documentation member lost their marrow graft after a transient neutrophil recovery beyond day 21 post transplant

E. PERIPHERAL BLOOD PROGENITOR CELL COLLECTION:
   1. Prescriber attests that member is in need of sargramostim therapy for the mobilization of autologous hematopoietic progenitor cells into the peripheral blood for collection by leukapheresis and will be initiated before leukapheresis (e.g., prescribed for 6 to 7 days with leukapheresis on days 5, 6 and 7)

F. DRUG OR HIV INDUCED NEUTROPENIA:
   1. Documentation patient is immunosuppressed and has a diagnosis of HIV disease
      AND
   2. Documentation member is concurrently taking ganciclovir or zidovudine
      AND
   3. Documentation member has an ANC ≤ 1,000 (cells/mm3) [DOCUMENTATION REQUIRED]

G. NEUROBLASTOMA:
   1. (a) Documentation member has a diagnosis of relapsed or refractory high-risk neuroblastoma in the bone or bone marrow
      AND
      (b) Prescriber attests sargramostim will be used concurrently with naxitamab
      OR
   2. (a) Documentation member has a diagnosis of pediatric high-risk neuroblastoma
      AND
      (b) Prescriber attests sargramostim will be used concurrently with Unituxin (dinutuximab)

H. ACUTE RADIATION SYNDROME:
   1. Documentation that member has had suspected or confirmed acute exposure to myelosuppressive doses of radiation [greater than 2 Grays (Gy)] [DOCUMENTATION REQUIRED]

CONTINUATION OF THERAPY:

A. FOR ALL INDICATIONS (FEBRILE NEUTROPENIA PROPHYLAXIS IN NON-MYELOID MALIGNANCIES AND AML ONLY, NEUROBLASTOMA):
   1. Member is compliant with sargramostim therapy as verified by prescriber and fill/claim history
      AND
   2. Documentation of clinical benefits to support continuation of treatment including positive response to therapy (i.e., member did not become neutropenic mid-cycle requiring G-CSF), low disease activity and/or improvements in the condition's signs and symptoms [DOCUMENTATION REQUIRED]
      AND
   3. Prescriber attests to regular lab monitoring (i.e., CBC and ANC) as clinically appropriate and rationale for medical necessity for continuation of therapy
      AND
   4. Prescriber attests to or clinical reviewer has found no evidence of intolerable adverse effects or drug toxicity

NOTE: Continuation of Therapy is not applicable to acute radiation syndrome, drug/HIV induced neutropenia, peripheral blood progenitor cell collection, febrile neutropenia prophylaxis following HSCT or treatment of delayed neutrophil recovery or graft failure – all requests for these indications must process through initial criteria.

DURATION OF APPROVAL:
Initial Authorization: 12 weeks, For oncology/chemotherapy related indications: Up to 12 weeks or up to length of chemotherapy approval date- whichever is shorter,
Continuation of Therapy: Up to 12 weeks or up to length of chemotherapy approval date- whichever is shorter
NOTE: Continuation of Therapy is not applicable to acute radiation syndrome, drug/HIV induced neutropenia, peripheral blood progenitor cell collection, febrile neutropenia prophylaxis following HSCT or treatment of delayed neutrophil recovery or graft failure – all requests for these indications must process through initial criteria.

PRESCRIBER REQUIREMENTS:
Prescribed by or in consultation with a board-certified hematologist, oncologist, infectious disease specialist or transplant specialist [If prescribed in consultation, consultation notes must be submitted with initial request and reauthorization requests]

AGE RESTRICTIONS:
One month of age and older

QUANTITY:
Must be prescribed within FDA labeled or compendia supported dosing maximums

PLACE OF ADMINISTRATION:
The recommendation is that injectable medications in this policy will be for pharmacy or medical benefit coverage and the subcutaneous injectable products administered in a place of service that isa non-hospital facility-based location.

The recommendation is that infused medications in this policy will be for pharmacy or medical benefit coverage administered in a place of service that is a non-inpatient hospital facility-based location.

DRUG INFORMATION

ROUTE OF ADMINISTRATION:
Intravenous or Subcutaneous

DRUG CLASS:
Granulocyte/Macrophage Colony-stimulating Factor (GM-CSF)

FDA-APPROVED USES:
LEUKINE is a leukocyte growth factor indicated:

- To shorten time to neutrophil recovery and to reduce the incidence of severe and life- threatening infection and infections resulting in death following induction chemotherapy in adult patients 55 years and older with acute myeloid leukemia (AML).
- For the mobilization of hematopoietic progenitor cells into peripheral blood for collection by leukapheresis and autologous transplantation in adult patients.
- For the acceleration of myeloid reconstitution following autologous bone marrow or peripheral blood progenitor cell transplantation in adult and pediatric patients 2 years of age and older.
- For the acceleration of myeloid reconstitution following allogeneic bone marrow transplantation in adult and pediatric patients 2 years of age and older.

- For treatment of delayed neutrophil recovery or graft failure after autologous or allogeneic bone marrow transplantation in adult and pediatric patients 2 years of age and older.
- 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 APPROVED OFF-LABELED USES:

Prophylaxis of febrile neutropenia in non-myeloid malignancies following myelosuppressive chemotherapy, Zidovudine-induced neutropenia, Ganciclovir-induced neutropenia, Aplastic anemia, Malignant melanoma, Myelodysplastic syndrome (MDS)

APPENDIX

APPENDIX:

A biosimilar is highly similar version of a brand name biological drug that meets strict controls for structural, pharmaceutical, and clinical consistency. A biosimilar manufacturer must demonstrate that there are no meaningful clinical differences (i.e., safety and efficacy) between the biosimilar and the reference product. Clinical performance is demonstrated through human pharmacokinetic (exposure) and pharmacodynamic (response) studies, an assessment of clinical immunogenicity, and, if needed, additional clinical studies.1

As costs for biological specialty drugs continue to rise, the growing biosimilar market will benefit providers and patients by broadening biological treatment options and expanding access to these medications at lower costs. Molina Healthcare, Inc. continues to be committed to continually reevaluating Preferred strategies and applying innovative cost-controls to ensure patients receive safe, effective and quality healthcare. This commitment includes potentially creating a preference for biosimilars when value can be added without compromising patient satisfaction and safety.

1. Food and Drug Administration. Biosimilar and Interchangeable Products. Retrieved from https://www.fda.gov/drugs/biosimilars/biosimilar- and- interchangeable-products. Accessed October 8, 2019.

ASCO Guidelines:
American Society of Clinical Oncology (ASCO) 2015 Recommendations for the use of WBC Growth Factors recommends primary CSF prophylaxis for patients who have an approximately 20% or higher risk for febrile neutropenia on the basis of patient, disease, and treatment related factors and patients receiving dose-dense chemotherapy.

NCCN Guideline Examples of Chemotherapy Regimens with a High Risk for Febrile Neutropenia (>20%)

National Comprehensive Cancer Network®

NCCN Guidelines Version 2.2024
Hematopoietic Growth Factors

NCCN Guidelines Index
Table of Contents
Discussion

EXAMPLES OF DISEASE SETTINGS AND CHEMOTHERAPY REGIMENS WITH A HIGH RISK FOR FEBRILE NEUTROPENIA (>20%)[a]

- ***This list is not comprehensive***; there are other agents/regimens that have a high risk for the development of febrile neutropenia. Regimens recommended in the NCCN Guidelines for Treatment by Cancer Type are considered when updating this list of examples.
- The type of chemotherapy regimen is only one component of the risk assessment (Patient Risk Factors for Developing Febrile Neutropenia, MGF-2).
- The exact risk includes agent, dose, and the treatment setting (ie, treatment naive vs. heavily pretreated patients) (MGF-1).
- In general, dose-dense regimens require MGF support to maintain dose intensity and schedule.

Acute Lymphoblastic Leukemia (ALL)
- Select ALL regimens as directed by treatment protocol (NCCN Guidelines for ALL)

Bladder Cancer
- Dose-dense MVAC (methotrexate, vinblastine, doxorubicin, cisplatin)[1]

Bone Cancer
- VAIA (vincristine, doxorubicin, ifosfamide, and dactinomycin)[2]
- VDC-IE (vincristine, doxorubicin or dactinomycin, and cyclophosphamide alternating with ifosfamide and etoposide)[3]
- Cisplatin/doxorubicin[4]
- VDC (cyclophosphamide, vincristine, doxorubicin or dactinomycin)[5]
- VIDE (vincristine, ifosfamide, doxorubicin or dactinomycin, etoposide)[6]

Breast Cancer
- Dose-dense AC followed by dose-dense paclitaxel (doxorubicin, cyclophosphamide, paclitaxel)[7,b]
- TAC (docetaxel, doxorubicin, cyclophosphamide)[8]
- TC[a,c] (docetaxel, cyclophosphamide)[9]
- TCH[a] (docetaxel, carboplatin, trastuzumab)[10]

Head and Neck Squamous Cell Carcinoma
- TPF (docetaxel, cisplatin, 5-fluorouracil)[11-13]

Hodgkin Lymphoma
- Brentuximab vedotin + AVD (doxorubicin, vinblastine, dacarbazine)[14]
- Escalated BEACOPP[d] (bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, prednisone)[15]

Kidney Cancer
- Doxorubicin/gemcitabine[16]

Non-Hodgkin Lymphomas
- CHP (cyclophosphamide, doxorubicin, prednisone) + brentuximab vedotin
- Dose-adjusted EPOCH[a] (etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin)[17]
- ICE (ifosfamide, carboplatin, etoposide)[a,18,19]
- Dose-dense CHOP-14[a] (cyclophosphamide, doxorubicin, vincristine, prednisone)[20,21]
- MINE[a] (mesna, ifosfamide, mitoxantrone, etoposide)[22]
- DHAP[a] (dexamethasone, cisplatin, cytarabine)[23]
- ESHAP[a] (etoposide, methylprednisolone, cisplatin, cytarabine)[24]
- HyperCVAD[a] (cyclophosphamide, vincristine, doxorubicin, dexamethasone)[25,26]
- Pola-R-CHP (polatuzumab vedotin-piiq, rituximab, cyclophosphamide, doxorubicin, prednisone)[27]

Melanoma
- Dacarbazine-based combination with IL-2, interferon alfa (dacarbazine, cisplatin, vinblastine, IL-2, interferon alfa)[28]

Multiple Myeloma
- DT-PACE (dexamethasone/thalidomide/cisplatin/doxorubicin/cyclophosphamide/etoposide)[29] ± bortezomib (VTD-PACE)[30]

Ovarian Cancer
- Topotecan[a,31]
- Docetaxel[32]

Soft Tissue Sarcoma
- MAID (mesna, doxorubicin, ifosfamide, dacarbazine)[33]
- Doxorubicin[a,34]
- Ifosfamide/doxorubicin[35]

Small Cell Lung Cancer[e]
- Topotecan[36]

Testicular Cancer
- VeIP (vinblastine, ifosfamide, cisplatin)[37]
- VIP (etoposide, ifosfamide, cisplatin)
- TIP (paclitaxel, ifosfamide, cisplatin)[38]

Disease Settings and Chemotherapy Regimens with an Intermediate Risk for Febrile Neutropenia, MGF-A (2 of 5)

[a] Guidelines apply to chemotherapy regimens with or without monoclonal antibodies (eg, trastuzumab, rituximab). There is the potential for increased neutropenia risk with the addition of monoclonal antibodies. Rituximab has been associated with prolonged neutropenia with or without chemotherapy. For details on when monoclonal antibodies are recommended with the regimens listed above in clinical practice, see NCCN Guidelines for Treatment by Cancer Type.

[b] Growth factor support may not be needed during the paclitaxel portion and can be safely avoided in a large percentage of patients.

[c] Risk for febrile neutropenia has been reported variably as intermediate risk or high risk depending on the study.

[d] Risk of bleomycin-induced pulmonary toxicity may be increased in patients treated with G-CSFs. See Toxicity Risks with MGFs (MGF-C).

[e] Trilaciclib may be used as a prophylactic option to decrease the incidence of chemotherapy-induced myelosuppression when administered before (prophylactic G-CSF may be administered after cycle 1) platinum/etoposide ± immune checkpoint inhibitor-containing regimens or a topotecan-containing regimen for extensive-stage small cell lung cancer (ES-SCLC).

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

References

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:
None

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:
All other uses of sargramostim are considered experimental/investigational and therefore, will follow Molina's Off-Label policy. Contraindications to Leukine (sargramostim) include: Patients with a history of serious allergic reactions, including anaphylaxis, to human granulocyte-macrophage colony-stimulating factor such as sargramostim, yeast-derived products, or any component of the product, avoid concomitant use with products that induce myeloproliferation (such as lithium and corticosteroids).

OTHER SPECIAL CONSIDERATIONS:
None

CODING/BILLING INFORMATION

Note: 1) This list of codes may not be all-inclusive. 2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement

HCPCS CODE	DESCRIPTION
J2820	injection, sargramostim (gm-csf), 50mcg

AVAILABLE DOSAGE FORMS:
Leukine SOLR 250MCG single-dose vial

REFERENCES

1. Leukine (sargramostim) for injection, for subcutaneous or intravenous use [prescribing information]. Lexington, MA; Partner Therapeutics, Inc.; August 2023.
2. Spitler LE, Grossbard ML, Ernstoff MS, et al. Adjuvant therapy of stage III and IV malignant melanoma using granulocyte-macrophage colony stimulating factor. J ClinOncol 2000;18:1614- 21.
3. US Public Health Service (USPHS) and the Infectious Diseases Society of America (IDSA). The Living Document: Guidelines for the Preventing Opportunistic Infections Among HIV-Infected Persons. Retrieved November 28, 2001. Available on the World Wide Web at www.aidsinfo.nih.gov.
4. Danyelza (naxitamab-gqgk) injection, for intravenous use [prescribing information]New York, NY: Y-mAbs Therapeutics, Inc; November 2020.
5. Unituxin (dinutuximab) injection, for intravenous use [prescribing information]. Research Triangle Park, NC; United Therapeutics Corp.; September 2020.
6. National Comprehensive Cancer Network. 2022. Hematopoietic Growth Factors (Version 1.2023). [online] Available at: < growthfactors.pdf (nccn.org)f> [Accessed 16 December 2022].
7. Smith, T. J., Bohlke, K., Lyman, G. H., Carson, K. R., Crawford, J., Cross, S. J., . . . Armitage, J. O. (2015). Recommendations for the use of WBC Growth Factors: American Society of Clinical Oncology Clinical Practice Guideline update. Journal of Clinical Oncology, 33(28), 3199-3212. doi:10.1200/jco.2015.62.3488
8. National Comprehensive Cancer Network. 2023. Hematopoietic Growth Factors (Version 2.2024). [online] Available at: <growthfactors.pdf (nccn.org)> [Accessed 14 December 2023].

SUMMARY OF REVIEW/REVISIONS	DATE
REVISION- Notable revisions: Required Medical Information Continuation of Therapy Duration of Approval References	Q1 2024
REVISION- Notable revisions: Diagnosis Required Medical Information Continuation of Therapy Duration of Approval Prescriber Requirements Compendial Approved Off-Labeled Uses Appendix Contraindications/Exclusions/Discontinuation References	Q1 2023
Q2 2022 Established tracking in new format	Historical changes on file