AETNA BETTER HEALTH®
Coverage Policy/Guideline

Name:	Leukine	Page:	1 of 8
Effective Date:	12/10/2024	Last Review Date:	11/19/2024
Applies to:	☒Florida Kids ☒Pennsylvania Kids	☒New Jersey ☒Virginia	☒Maryland ☒Kentucky PRMD

Intent:

The intent of this policy/guideline is to provide information to the prescribing practitioner outlining the coverage criteria for Leukine under the patient's prescription drug benefit.

Description:

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.

A. FDA-Approved Indications
   1. 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).
   2. 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.
   3. 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).
   4. 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.
   5. 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.
   6. 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]).

B. Compendial Uses
   1. Prophylaxis and treatment of chemotherapy-induced febrile neutropenia in non-myeloid malignancies

2. Treatment of neutropenia and anemia in patients with myelodysplastic syndromes (MDS)
3. Acute myeloid leukemia
4. Agranulocytosis (non-chemotherapy drug induced)
5. Aplastic anemia
6. Neutropenia related to HIV/AIDS
7. Stem cell transplantation-related indications
8. Neuroblastoma
9. Severe chronic neutropenia (congenital, cyclic, or idiopathic)

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

Applicable Drug List:

Leukine

Policy/Guideline:

Documentation:
Primary Prophylaxis of Febrile Neutropenia

1. Documentation must be provided of the member's diagnosis and chemotherapeutic regimen.
2. If chemotherapeutic regimen has an intermediate risk of febrile neutropenia (10-19% [See Appendix B]), documentation must be provided outlining the member's risk factors that confirm the member is at high risk for febrile neutropenia.

Criteria for Initial Approval:

Note: Requests for Leukine require patient is unable to take Zarxio for the given diagnosis due to a trial and inadequate treatment response or intolerance, or a contraindication for all indications except neuroblastoma.

A. Neutropenia in cancer patients receiving myelosuppressive chemotherapy
Authorization of 6 months may be granted for prevention or treatment of febrile neutropenia when ALL the following criteria are met (1, 2, and 3):

1. The requested medication will not be used in combination with other colony stimulating factors within any chemotherapy cycle.
2. The member will not receive chemotherapy at the same time as they receive radiation therapy.
3. ONE of the following criteria is met (i, ii, or iii):
   i. 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:

a. Myelosuppressive anti-cancer therapy that is expected to result in 20% or higher incidence of
febrile neutropenia (FN) *(See Appendix A)*.
b. 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*).
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)*.

ii. 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).

iii. 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:
a. Age greater than 65 years
b. Being hospitalized at the time of the development of fever
c. Sepsis syndrome
d. Invasive fungal infection
e. Pneumonia or other clinically documented infection
f. Prolonged (neutropenia expected to last greater than 10 days) or profound (absolute neutrophil count less than 0.1 x 10^9/L) neutropenia
g. Prior episodes of febrile neutropenia

B. Neuroblastoma

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

1. Dinutuximab (Unituxin) and isotretinoin (13-cis-retinoic acid [RA])
2. Temozolomide, irinotecan, and dinutuximab (Unituxin)
3. Naxitamab-gqgk (Danyelza)

C. Other indications

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

1. Myelodysplastic syndrome (anemia or neutropenia)
2. Acute myeloid leukemia
3. Agranulocytosis (non-chemotherapy drug induced)

4. Aplastic anemia
5. Neutropenia related to HIV/AIDS
6. Stem cell transplantation-related indications
7. Severe chronic neutropenia (congenital, cyclic, or idiopathic)
8. 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:

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

1. Acute Lymphoblastic Leukemia:
   Select ALL regimens as directed by treatment protocol (see NCCN guidelines ALL)
2. Bladder Cancer:
   i. Dose dense MVAC (methotrexate, vinblastine, doxorubicin, cisplatin)
3. Bone Cancer:
   i. VAI (vincristine, doxorubicin or dactinomycin, ifosfamide)
   ii. VDC-IE (vincristine, doxorubicin or dactinomycin, and cyclophosphamide alternating with ifosfamide and etoposide)
   iii. Cisplatin/doxorubicin
   iv. VDC (cyclophosphamide, vincristine, doxorubicin or dactinomycin)
   v. VIDE (vincristine, ifosfamide, doxorubicin or dactinomycin, etoposide)
4. Breast Cancer:
   i. Dose-dense AC (doxorubicin, cyclophosphamide) followed by dose-dense paclitaxel
   ii. TAC (docetaxel, doxorubicin, cyclophosphamide)
   iii. TC (docetaxel, cyclophosphamide)
   iv. TCH (docetaxel, carboplatin, trastuzumab)
5. Head and Neck Squamous Cell Carcinoma
   TPF (docetaxel, cisplatin, 5-fluorouracil)
6. Hodgkin Lymphoma:
   i. Brentuximab vedotin + AVD (doxorubicin, vinblastine, dacarbazine)

ii. Escalated BEACOPP (bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, prednisone)

7. Kidney Cancer:
   Doxorubicin/gemcitabine

8. Non-Hodgkin's Lymphoma:
   i. CHP (cyclophosphamide, doxorubicin, prednisone) + brentuximab vedotin
   ii. Dose-adjusted EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin)
   iii. ICE (ifosfamide, carboplatin, etoposide)
   iv. Dose-dense CHOP-14 (cyclophosphamide, doxorubicin, vincristine, prednisone) ± rituximab
   v. MINE (mesna, ifosfamide, mitoxantrone, etoposide)
   vi. DHAP (dexamethasone, cisplatin, cytarabine)
   vii. ESHAP (etoposide, methylprednisolone, cisplatin, cytarabine (Ara-C))
   viii. HyperCVAD ± rituximab (cyclophosphamide, vincristine, doxorubicin, dexamethasone ± rituximab)
   ix. Pola-R-CHP (polatuzumab vedotin-piiq, rituximab, cyclophosphamide, doxorubicin, prednisone)

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

10. Multiple Myeloma:
    i. VTD-PACE (dexamethasone/thalidomide/cisplatin/doxorubicin/cyclophosphamide/etoposide + bortezomib)
    ii. DT-PACE (dexamethasone/thalidomide/cisplatin/doxorubicin/cyclophosphamide/etoposide)

11. Ovarian Cancer:
    i. Topotecan
    ii. Docetaxel

12. Soft Tissue Sarcoma:
    i. MAID (mesna, doxorubicin, ifosfamide, dacarbazine)
    ii. Doxorubicin
    iii. Ifosfamide/doxorubicin

13. Small Cell Lung Cancer:
    Top (topotecan)

14. Testicular Cancer:

i. VelP (vinblastine, ifosfamide, cisplatin)
ii. VIP (etoposide, ifosfamide, cisplatin)
iii. TIP (paclitaxel, ifosfamide, cisplatin)

15. Gestational Trophoblastic Neoplasia:
    i. EMA/CO (etoposide, methotrexate, dactinomycin/cyclophosphamide, vincristine)
    ii. EMA/EP (etoposide, methotrexate, dactinomycin/etoposide, cisplatin)
    iii. EP/EMA (etoposide, cisplatin/etoposide, methotrexate, dactinomycin)
    iv. TP/TE (paclitaxel, cisplatin/paclitaxel, etoposide)
    v. BEP (bleomycin, etoposide, cisplatin)
    vi. VIP (etoposide, ifosfamide, cisplatin)
    vii. ICE (ifosfamide, carboplatin, etoposide)

16. Wilms Tumor:
    i. Regimen M (vincristine, dactinomycin, doxorubicin, cyclophosphamide, etoposide)
    ii. 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.

B. APPENDIX B:
<u>Selected Chemotherapy Regimens with an Incidence of Febrile Neutropenia of 10% to 19%</u>*†

1. Occult Primary – Adenocarcinoma:
   Gemcitabine/docetaxel

2. Breast Cancer:
    i. Docetaxel
    ii. CMF classic (cyclophosphamide, methotrexate, fluorouracil)
    iii. AC (doxorubicin, cyclophosphamide) + sequential docetaxel (taxane portion only)
    iv. AC + sequential docetaxel + trastuzumab
    v. Paclitaxel every 21 days ± trastuzumab
    vi. TC (docetaxel, cyclophosphamide)

3. Cervical Cancer:
    i. Irinotecan
    ii. Cisplatin/topotecan
    iii. Paclitaxel/cisplatin ± bevacizumab

iv. Topotecan

4. Colorectal Cancer:
   FOLFIRINOX (fluorouracil, leucovorin, oxaliplatin, irinotecan)
5. Esophageal and Gastric Cancers:
   Irinotecan/cisplatin
6. Non-Hodgkin's Lymphomas:
   i. GDP (gemcitabine, dexamethasone, cisplatin/carboplatin)
   ii. GDP (gemcitabine, dexamethasone, cisplatin/carboplatin) + rituximab
   iii. CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) including regimens with pegylated liposomal doxorubicin
   iv. CHOP + rituximab (cyclophosphamide, doxorubicin, vincristine, prednisone, rituximab) including regimens with pegylated liposomal doxorubicin
   v. Bendamustine
7. Non-Small Cell Lung Cancer:
   i. Cisplatin/paclitaxel
   ii. Cisplatin/vinorelbine
   iii. Cisplatin/docetaxel
   iv. Cisplatin/etoposide
   v. Carboplatin/paclitaxel
   vi. Docetaxel
8. Ovarian Cancer:
   Carboplatin/docetaxel
9. Pancreatic Cancer:
   FOLFIRINOX (fluorouracil, leucovorin, oxaliplatin, irinotecan)
10. Prostate Cancer:
    Cabazitaxel
11. Small Cell Lung Cancer:
    Etoposide/carboplatin
12. Testicular Cancer:
    i. BEP (bleomycin, etoposide, cisplatin)
    ii. Etoposide/cisplatin
13. 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.

C. 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

Approval Duration and Quantity Restrictions:

Approval: 6 months

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