Reference number(s)
1929-A

SPECIALTY GUIDELINE MANAGEMENT

LEUKINE (sargramostim)

POLICY

I. 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.

A. FDA-Approved Indications
   A. Use Following Induction Chemotherapy in Acute Myelogenous Leukemia
      Leukine is indicated for use following induction chemotherapy in adult patients 55 years and older with acute myelogenous leukemia (AML) to shorten time to neutrophil recovery and to reduce the incidence of severe and life-threatening infections and infections resulting in death.
   B. 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.
   C. 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).
   D. Allogeneic Bone Marrow Transplantation (BMT)
      Leukine is indicated for 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.
   E. 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.
   F. 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)

10. Radiation therapy/injury

All other indications are considered experimental/investigational and are not a covered benefit.

II. REQUIRED DOCUMENTATION

Primary Prophylaxis of Febrile Neutropenia

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

III. CRITERIA FOR INITIAL APPROVAL

A. 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):

1. The requested medication will not be used in combination with other colony stimulating factors within any chemotherapy cycle.
2. The member will not be receiving concurrent chemotherapy and 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 myelosuppressive anti-cancer therapy that is expected to result in 20% or higher incidence of FN *(See Appendix A)* OR 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-morbidity, including any of the following (not an all-inclusive list):
        a. Active infections, open wounds, or recent surgery
        b. Age greater than or equal to 65 years
        c. Bone marrow involvement by tumor producing cytopenias
        d. Previous chemotherapy or radiation therapy
        e. Poor nutritional status
        f. Poor performance status
        g. Previous episodes of FN
        h. Other serious co-morbidities, including renal dysfunction, liver dysfunction, HIV infection, cardiovascular disease
        i. Persistent neutropenia
    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 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 1 x 10^9/L) neutropenia

g. Prior episodes of febrile neutropenia

B. 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. Neuroblastoma
   Use with dinutuxin (Unituxin), interleukin-2 (aldesleukin (Proleukin)), and isotretinoin (13-cis-retinoic acid (RA)), for the treatment of high-risk neuroblastoma.
8. Severe chronic neutropenia (congenital, cyclic, or idiopathic)
9. Radiation therapy/injury
   i. Manage neutropenia in members acutely exposed to myelosuppressive doses of radiation therapy
   ii. Treatment of radiation injury

IV. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

V. 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)
2. Bladder Cancer:
   i. Dose dense MVAC (methotrexate, vinblastine, doxorubicin, cisplatin)
   ii. CBDCa/Pac (carboplatin, paclitaxel)
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. Docetaxel + trastuzumab
   ii. Dose-dense AC (doxorubicin, cyclophosphamide) + paclitaxel (or dose dense paclitaxel)
   iii. TAC (docetaxel, doxorubicin, cyclophosphamide)
   iv. AT (doxorubicin, docetaxel)
   v. Doc (docetaxel)
   vi. TC (docetaxel, cyclophosphamide)
   vii. TCH (docetaxel, carboplatin, trastuzumab)
5. Colorectal Cancer:

FOLFOXIRI (fluorouracil, leucovorin, oxaliplatin, irinotecan)

6. Esophageal and Gastric Cancers:
   Docetaxel/cisplatin/fluorouracil
7. Head and Neck Squamous Cell Carcinoma
   TPF (docetaxel, cisplatin, fluorouracil)
8. Hodgkin Lymphoma:
   i. Brentuximab vedotin + AVD (doxorubicin, vinblastine, dacarbazine)
   ii. Escalated BEACOPP (bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, prednisone)
9. Kidney Cancer:
   Doxorubicin/gemcitabine
10. Non-Hodgkin's Lymphoma:
    i. Dose-adjusted EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin)
    ii. ICE (ifosfamide, carboplatin, etoposide)
    iii. Dose-dense CHOP-14 (cyclophosphamide, doxorubicin, vincristine, prednisone) + rituximab
    iv. MINE (mesna, ifosfamide, novantrone, etoposide)
    v. DHAP (dexamethasone, cisplatin, cytarabine)
    vi. ESHAP (etoposide, methylprednisolone, cisplatin, cytarabine (Ara-C))
    vii. HyperCVAD + rituximab (cyclophosphamide, vincristine, doxorubicin, dexamethasone + rituximab)
    viii. VAPEC-B (vincristine, doxorubicin, prednisolone, etoposide, cyclophosphamide, bleomycin)
11. Melanoma:
    Dacarbazine-based combination with IL-2, interferon alpha (dacarbazine, cisplatin, vinblastine, IL-2, interferon alpha)
12. Multiple myeloma:
    i. DT-PACE (dexamethasone/ thalidomide/ cisplatin/ doxorubicin/ cyclophoaphamide/ etoposide) + bortezomib (VTD-PACE)
    ii. DT-PACE (dexamethasone/thalidomide/cisplatin/doxorubicin/cyclophoaphamide/etoposide)
13. Ovarian Cancer:
    i. Topotecan
    ii. Docetaxel
14. Pancreatic Cancer:
    FOLFIRINOX (fluorouracil, leucovorin, irinotecan, oxaliplatin)
15. Soft Tissue Sarcoma:
    i. MAID (mesna, doxorubicin, ifosfammide, dacarbazine)
    ii. Doxorubicin
    iii. Ifosfamide/doxorubicin
16. Small Cell Lung Cancer:
    i. Top (topotecan)
    ii. CAV (cyclophosphamide, doxorubicin, vincristine)
17. Testicular cancer:
    i. VelP (vinblastine, ifosfamide, cisplatin)
    ii. VIP (etoposide, ifosfamide, cisplatin)
    iii. TIP (paclitaxel, ifosfamide, cisplatin)

B. <u>APPENDIX B: 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. CA (doxorubicin, cyclophosphamide) (60 mg/m2) (hospitalized)
   iv. AC (doxorubicin, cyclophosphamide) + sequential docetaxel (taxane portion only)
   v. AC + sequential docetaxel + trastuzumab
   vi. A (doxorubicin) (75 mg/m2)
   vii. AC (doxorubicin, cyclophosphamide)
   viii. CapDoc (capecitabine, docetaxel)
   ix. Paclitaxel every 21 days
3. Cervical Cancer:
   i. Irinotecan
   ii. Cisplatin/topotecan
   iii. Paclitaxel/cisplatin
   iv. Topotecan
4. Colorectal:
   i. FL (fluorouracil, leucovorin)
   ii. CPT-11 (irinotecan) (350 mg/m2 q 3 wk)
   iii. FOLFOX (fluorouracil, leucovorin, oxaliplatin)
5. Esophageal and Gastric Cancers:
   i. Irinotecan/cisplatin
   ii. Epirubicin/cisplatin/fluorouracil
   iii. Epirubicin/cisplatin/capecitabine
6. Non-Hodgkin's lymphomas:
   i. EPOCH-IT chemotherapy
   ii. GDP (gemcitabine, dexamethasone, cisplatin/carboplatin)
   iii. GDP (gemcitabine, dexamethasone, cisplatin/carboplatin) + rituximab
   iv. FMR (fludarabine, mitoxantrone, rituximab)
   v. CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) including regimens with pegylated liposomal doxorubicin
   vi. CHOP + rituximab (cyclophosphamide, doxorubicin, vincristine, prednisone, rituximab) including regimens with pegylated liposomal doxorubicin
   vii. CHP (cyclophosphamide, doxorubicin, prednisone) + brentuximab vedotin
   viii. 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. Prostate cancer:
   Cabazitaxel
10. Small Cell Lung Cancer:
    Etoposide/carboplatin
11. Testicular Cancer:
    i. BEP (bleomycin, etoposide, cisplatin)

ii. Etoposide/cisplatin

12. Uterine sarcoma:
    Docetaxel

VI. REFERENCES

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