Colony-Stimulating Factors

Generic Name: Colony-Stimulating Factors

Therapeutic Class or Brand Name: Colony-Stimulating Factors

Applicable Drugs (if Therapeutic Class): Fulphila™ (pegfilgrastim-jmdb), Granix® (tbo-filgrastim), Leukine® (sargramostim), Neupogen® (filgrastim), Neulasta® (pegfilgrastim), Nivestym™ (filgrastim-aafi), Zarxio™ (filgrastim-sndz).

GPI Code: 8240152000, 8240152060, 8240152070, 8240157000, 8240205000

Preferred: Granix® (tbo-filgrastim)

Non-preferred: Fulphila™ (pegfilgrastim-jmdb), Leukine® (sargramostim), Neupogen® (filgrastim), Neulasta® (pegfilgrastim), Nivestym™ (filgrastim-aafi), Zarxio™ (filgrastim-sndz).

Date of Origin: 2/1/2013

Date Last Reviewed / Revised: 10/22/2018

PRIOR AUTHORIZATION CRITERIA

(May be considered medically necessary when criteria I through III are met)

I. Documented diagnosis of one of the following A through J AND must meet criteria listed under applicable diagnosis:

A. Primary prophylaxis of chemotherapy-induced neutropenia when myelosuppressive chemotherapy is used for the treatment of a solid tumor or a non-myeloid malignancy (malignancies other than myeloid leukemias) and ONE of the following criteria 1 or 2 is met:

1. The chemotherapy regimen has a high risk (20% or greater) for febrile neutropenia (see Appendix).
2. Documentation that the member is at high risk for developing febrile neutropenia by meeting at least ONE of the following criteria a through h:
   a. Age is at least 65 years old.
   b. Previous chemotherapy or radiation therapy.
   c. Preexisting neutropenia or bone marrow involvement with tumor.
   d. Preexisting conditions such as neutropenia, infection/open wounds, or recent surgery.
   e. Poor performance status.
   f. Poor renal function.
   g. Liver dysfunction, most notably elevated bilirubin.
   h. HIV-infected.

B. Secondary Prophylaxis of chemotherapy-induced neutropenia when neutropenic complications (i.e. infection, febrile neutropenia) were experienced with a prior cycle of

chemotherapy and a reduction in the chemotherapy dose or a delay in therapy is inappropriate.

C. Following induction or consolidation chemotherapy used for the treatment of acute myeloid leukemia (AML) to reduce the time to neutrophil recovery, the duration of fever, and the incidence of severe and life-threatening infections.

D. Priming collection and mobilization of peripheral-blood stem cells for harvest prior to autologous transplantation.

E. Acceleration of neutrophil recovery following stem cell transplant.

F. Neutropenia in conjunction with high-dose chemotherapy with autologous stem cell support.

G. Congenital, idiopathic, or cyclic neutropenia with clinically significant episodes of recurrent fevers, infection, and/or oropharyngeal ulcers.

H. Patients who have undergone allogeneic or autologous bone marrow transplantation and are experiencing graft failure or delayed engraftment in the presence or absence of infection.

I. Drug-induced neutropenia in HIV-infected patients when an alternative to the offending agent is not available, not tolerated, or is less effective.

J. Neutropenia in patients with myelodysplastic syndrome.

II. Prescribing physician must be a hematologist or oncologist.

III. Non-preferred products require a documented clinical reason why the member cannot use the preferred product(s).

Exclusion Criteria

- Prevention of cytopenia in patients who are scheduled for, but not receiving, myelosuppressive chemotherapy.
- Treatment of chronic marrow failure (low white blood cell counts) due to prior chemotherapy treatment.
- Treatment of drug-induced neutropenias other than those causes listed above under Prior Authorization Criteria.

Other Criteria

- N/A

Quantity / Days Supply Restrictions

- The quantity is limited to a maximum of a 30 day supply per fill.

APPROVAL LENGTH

- **Authorization:** 6 months.
- **Re-Authorization:** An updated letter of medical necessity or progress notes showing current medical necessity criteria are met and that the medication is effective.

APPENDIX

Disease Settings and Chemotherapy Regimens with a High Risk for Febrile Neutropenia (≥ 20%)*

Acute Lymphoblastic Leukemia (ALL)

- ALL induction regimens, including but not limited to:
  - Imatinib or dasatinib and cyclophosphamide, vincristine, doxorubicin, dexamethasone
  - Imatinib and daunorubicin, vincristine, prednisone, cyclophosphamide
  - Daunorubicin, vincristine, prednisone, pegaspargase, cyclophosphamide

Bladder Cancer

- Dose-dense MVAC (methotrexate, vinblastine, doxorubicin, cisplatin) (neoadjuvant, adjuvant, metastatic)

Breast Cancer

- Dose-dense AC followed by T (doxorubicin, cyclophosphamide, paclitaxel) (adjuvant)
- TAC (docetaxel, doxorubicin, cyclophosphamide) (adjuvant)
- TC (docetaxel, cyclophosphamide)
- TCH (docetaxel, carboplatin,

Non-Hodgkin's Lymphomas (cont.)

- Dose-dense CHOP-14 (cyclophosphamide, doxorubicin, vincristine, prednisone)
- MINE (mesna, ifosfamide, novantrone, etoposide) (DLBCL, PTCL, 2nd line, refractory)
- DHAP (dexamethasone, cisplatin, cytarabine) (peripheral T-cell lymphomas, diffuse large B-cell lymphoma, 2nd line)
- ESHAP (etoposide, methylprednisolone, cisplatin, cytarabine) (DLBCL, PTCL, 2nd line, recurrent)
- HyperCVAD (cyclophosphamide, vincristine, doxorubicin, dexamethasone)

Melanoma

- Dacarbazine-based combination with IL-2, interferon alfa (dacarbazine, cisplatin, vinblastine, IL-2, interferon alfa) (advanced, metastatic, or recurrent)

Myelodysplastic Syndromes

- Antithymocyte globulin,

Disease Settings and Chemotherapy Regimens with a High Risk for Febrile Neutropenia (≥ 20%)*	
trastuzumab) Esophageal and Gastric Cancers • Docetaxel/cisplatin/fluorouracil Hodgkin Lymphoma • Escalated BEACOPP (bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, prednisone) Kidney Cancer • Doxorubicin/gemcitabine Non-Hodgkin's Lymphomas • CFAR (cyclophosphamide, fludarabine, alemtuzumab, rituximab) (CLL with del(17p), relapsed/refractory) • Dose-adjusted EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin) • ICE (ifosfamide, carboplatin, etoposide) (DLBCL, PTCL, 2nd line, salvage)	rabbit/cyclosporine • Decitabine Ovarian Cancer • Topotecan • Docetaxel Soft Tissue Sarcoma • MAID (mesna, doxorubicin, ifosfamide, dacarbazine) • Doxorubicin • Ifosfamide/doxorubicin Small Cell Lung Cancer • Topotecan Testicular cancer • VeIP (vinblastine, ifosfamide, cisplatin) • VIP (etoposide, ifosfamide, cisplatin) • BEP (bleomycin, etoposide, cisplatin) • TIP (paclitaxel, ifosfamide, cisplatin)
*This list is not comprehensive. Additional regimens may be considered for coverage if listed in the current NCCN guidelines (http://www.nccn.org/professionals/physician_gls/pdf/myeloid_growth.pdf) or the EORTC guidelines.	

REFERENCES

1. http://www.nccn.org/professionals/physician_gls/pdf/myeloid_growth.pdf .
2. http://blue.regence.com/trgmedpol/drugs/dru319.pdf .
3. https://www.capbluecross.com/wps/wcm/connect/prod_nws.capblue.com29556/1e311276-ebdb-4db7-802b-e3887f120e89/medical-policy-2-101.pdf?MOD=AJPERES&CVID=lMdBmce .
4. Medi-Span®.
5. http://products.sanofi.us/Leukine/Leukine.html .
6. http://pi.amgen.com/united_states/neupogen/neupogen_pi_hcp_english.pdf .
7. http://pi.amgen.com/united_states/neulasta/neulasta_pi_hcp_english.pdf .
8. http://www.granixhcp.com/Pdf/prescribing-information.pdf .
9. https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=fe707775-a0ae-41b5-a744-28c41889fce8&type=display .
10. https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/761075s000lbl.pdf .
11. https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/761080s000lbl.pdf .
12. https://www.accessdata.fda.gov/drugsatfda_docs/label/2015/125553lbl.pdf .

HISTORICAL TRACKING OF CHANGES MADE TO POLICY

Date	Notes/Changes
10/22/2018	1. **Added:** Fulfila™, Nivestym™, Zarxio™ to list of Applicable Drugs and Non-Preferred products. 2. **Added:** References #10-#12 for Fulfila™, Nivestym™, Zarxio™ package inserts. 3. **Added:** registered trademark symbol for reference #4 Medi-Span.
12/1/2017	1. **Added** "Breast Cancer: TC (docetaxel, cyclophosphamide)", "Breast Cancer: TCH (docetaxel, carboplatin, trastuzumab)", **and** "Non-Hodgkin's Lymphomas: Dose-adjusted EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin)" **to table under Appendix**. 2. **Changed** "Bladder Cancer: MVAC…" **to** "Bladder Cancer: Dose-dense MVAC…", "Hodgkin Lymphoma: BEACOPP…" **to** "Hodgkin Lymphoma: Escalated BEACOPP…", "Non-Hodgkin's Lymphomas: CHOP-14 (cyclophosphamide, doxorubicin, vincristine, prednisone) ± rituximab" **to** "Non-Hodgkin's Lymphomas: Dose-dense CHOP-14 (cyclophosphamide, doxorubicin, vincristine, prednisone)", **and** "Non-Hodgkin's Lymphomas: HyperCVAD + rituximab (cyclophosphamide, vincristine, doxorubicin, dexamethasone + rituximab)" **to** "Non-Hodgkin's Lymphomas: HyperCVAD (cyclophosphamide, vincristine, doxorubicin, dexamethasone)" **on table under Appendix**. 3. **Removed** "Breast Cancer: Docetaxel + trastuzumab (metastatic or relapsed)", "Non-Hodgkin's Lymphomas: RICE (rituximab, ifosfamide, carboplatin, etoposide)", "Melanoma: Dacarbazine-based combination (dacarbazine, cisplatin, vinblastine) (advanced, metastatic, or recurrent)", **and** "Ovarian Cancer: Paclitaxel" **from table under Appendix**. 4. **Removed** "http://www.elsevier.com/__data/assets/pdf_file/0020/115724/european-journal-of-cancer-article-3.pdf" **from table under Appendix** (link no longer valid). 5. **Updated** "https://www.capbluecross.com/wps/wcm/connect/37ab5e85-3caf-4429-a05c-

	853c1622937c/Colony-Stimulating+Factors+(GCSF+and+GM-CSF)+and+Stem+Cell+Mobilizers+consensus+3-26-13+SC.pdf?MOD=AJPERES" **to** "https://www.capbluecross.com/wps/wcm/connect/prod_nws.capblue.com29556/1e311276-ebdb-4db7-802b-e3887f120e89/medical-policy-2-101.pdf?MOD=AJPERES&CVID=lMdBmce" **under References**.
9/20/2016	1. **Added** "Zarxio® (filgrastim-sndz)" following "Non-Preferred" **under Applicable Drugs**. 2. **Added** "8240152060" **following GPI Code**. 3. **Changed** "Documented diagnosis of one of the following uses A through K…" **to** "Documented diagnosis of one of the following A through J…" **and removed** "K. Neutropenia secondary to hypersplenism" **under Prior Authorization Criteria**. 4. **Changed** "III. Non-preferred products (i.e. Leukine®, Neupogen®, Neulasta®) require a documented clinical reason why the member cannot use the preferred product Granix®" **to** "III. Non-preferred products require a documented clinical reason why the member cannot use the preferred product(s)" **under Prior Authorization Criteria**. 5. **Added** "Decitabine" below "Myelodysplastic Syndromes" **on Table under Appendix**. 6. **Removed** "https://medicaid.utah.gov/pharmacy/priorauthorization/pdf/NeupogenNeulastaLeukine.pdf" **from References** (link no longer valid). 7. **Added** "https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=fe707775-a0ae-41b5-a744-28c41889fce8&type=display" **under References**.
3/3/2015	1. **Changed** "Leukine® (sargramostim), Neupogen® (filgrastim), and Neulasta® (pegfilgrastim)" **to** "Preferred: Granix® (tbo-filgrastim); Non-Preferred: Leukine® (sargramostim), Neupogen® (filgrastim), Neulasta® (pegfilgrastim)" **under Applicable Drugs**. 2. **Added** "8240152070**" to list following GPI Code**. 3. **Changed Prior Authorization Criteria from**: "Prior Authorization Criteria (may be considered medically necessary when criterion I is met): I. Documented diagnosis of one of the following uses A through J: A. To elevate the white blood cell count in conjunction with high-dose chemotherapy with autologous stem cell support; B. To decrease the duration of neutropenia-related sequelae (such as febrile neutropenia) in patients with non-myeloid malignancies receiving myeloablative chemotherapy using cancer drugs which are known to cause severe neutropenia; C. To treat patients with congenital, idiopathic or cyclic neutropenia with clinically significant episodes of recurrent fevers, infection and/or oropharyngeal ulcers; D. Following induction chemotherapy in older adult patients with acute myelogenous leukemia to shorten time to neutrophil recovery and to reduce the incidence of severe and life-threatening infections; E. In patients who have undergone allogeneic or autologous bone marrow transplantation and are experiencing graft failure or delayed engraftment in the presence or absence of infection; F. To accelerate recovery of white blood cell counts and reduce incidence of infection after high-dose chemotherapy with allogeneic bone marrow transplantation; G. For use in priming collection and mobilization of peripheral blood stem cells; H. To treat drug-induced neutropenia in HIV-infected patients when an alternative(s) to the offending agent is not available, not tolerated or is less effective; I. To increase neutrophil counts in patients with myelodysplastic syndrome; J. To treat neutropenia secondary to hypersplenism" **to:** "Prior Authorization Criteria (may be considered medically necessary when criteria I through III are met): I. I. Documented diagnosis of one of the following uses A through K AND must meet criteria listed under applicable diagnosis: A. Primary prophylaxis of chemotherapy-induced neutropenia when myelosuppressive chemotherapy is used for the treatment of a solid tumor or a non-myeloid malignancy (malignancies other than myeloid leukemias) and ONE of the following criteria 1 or 2 is met: 1. The chemotherapy regimen has a high risk (20% or greater)

	for febrile neutropenia (see Appendix); 2. Documentation that the member is at high risk for developing febrile neutropenia by meeting at least ONE of the following criteria a through h: a. Age is at least 65 years old; b. Previous chemotherapy or radiation therapy; c. Preexisting neutropenia or bone marrow involvement with tumor; d. Preexisting conditions such as neutropenia, infection/open wounds or recent surgery; e. Poor performance status; f. Poor renal function; g. Liver dysfunction, most notably elevated bilirubin; h. HIV-infected; B. Secondary Prophylaxis of chemotherapy-induced neutropenia when neutropenic complications (i.e. infection, febrile neutropenia) were experienced with a prior cycle of chemotherapy and a reduction in the chemotherapy dose or a delay in therapy is inappropriate; C. Following induction or consolidation chemotherapy used for the treatment of acute myeloid leukemia (AML) to reduce the time to neutrophil recovery, the duration of fever, and the incidence of severe and life-threatening infections; D. Priming collection and mobilization of peripheral-blood stem cells for harvest prior to autologous transplantation; E. Acceleration of neutrophil recovery following stem cell transplant; F. Neutropenia in conjunction with high-dose chemotherapy with autologous stem cell support; G. Congenital, idiopathic, or cyclic neutropenia with clinically significant episodes of recurrent fevers, infection, and/or oropharyngeal ulcers; H. Patients who have undergone allogeneic or autologous bone marrow transplantation and are experiencing graft failure or delayed engraftment in the presence or absence of infection; I. Drug-induced neutropenia in HIV-infected patients when an alternative to the offending agent is not available, not tolerated, or is less effective; J. Neutropenia in patients with myelodysplastic syndrome; K. Neutropenia secondary to hypersplenism; II. Prescribing physician must be a hematologist or oncologist; III. Non-preferred products (i.e. Leukine®, Neupogen®, Neulasta®) require a documented clinical reason why the member cannot use the preferred product Granix®". 4. **Changed** "Treating chronic marrow failure (low white blood cell counts) due to prior chemotherapy treatment; To treat drug-induced neutropenias other than those causes listed above under Prior Authorization Criteria" **to** "Treatment of chronic marrow failure (low white blood cell counts) due to prior chemotherapy treatment; Treatment of drug-induced neutropenias other than those causes listed above under Prior Authorization Criteria" **under Exclusion Criteria**. 5. **Added** "Disease Settings and Chemotherapy Regimens with a High Risk for Febrile Neutropenia (> 20%)*" **table under Appendix**. 6. **Added** "http://www.nccn.org/professionals/physician_gls/pdf/myeloid_growth.pdf"**,** "http://blue.regence.com/trgmedpol/drugs/dru319.pdf"**, and** "http://www.granixhcp.com/Pdf/prescribing-information.pdf" **under References**. 7. **Updated** "http://www.health.utah.gov/medicaid/pharmacy/priorauthorization/pdf/NeupogenNeulastaLeukine.pdf" **to** "https://medicaid.utah.gov/pharmacy/priorauthorization/pdf/NeupogenNeulastaLeukine.pdf" **under References**.
12/9/2013	1. **Adapted policy to new format.** 2. **Added GPI Codes**. 3. **Changed Prior Authorization Criteria from:** "Documentation of one of the Covered Uses listed below: Myelosuppressive chemotherapy, bone marrow transplant, peripheral blood progenitor cell collection, or severe chronic neutropenia; OR ANC < 750 cells/microliter in patients with Hepatitis C who are being treated with Interferon." **to:** "Documented diagnosis of one of the following uses A through J: A. To elevate the white blood cell count in conjunction with high-dose chemotherapy with autologous stem cell

	support; B. To decrease the duration of neutropenia-related sequelae (such as febrile neutropenia) in patients with non-myeloid malignancies receiving myeloablative chemotherapy using cancer drugs which are known to cause severe neutropenia; C. To treat patients with congenital, idiopathic or cyclic neutropenia with clinically significant episodes of recurrent fevers, infection and/or oropharyngeal ulcers; D. Following induction chemotherapy in older adult patients with acute myelogenous leukemia to shorten time to neutrophil recovery and to reduce the incidence of severe and life-threatening infections; E. In patients who have undergone allogeneic or autologous bone marrow transplantation and are experiencing graft failure or delayed engraftment in the presence or absence of infection; F. To accelerate recovery of white blood cell counts and reduce incidence of infection after high-dose chemotherapy with allogeneic bone marrow transplantation; G. For use in priming collection and mobilization of peripheral blood stem cells; H. To treat drug-induced neutropenia in HIV-infected patients when an alternative(s) to the offending agent is not available, not tolerated or is less effective; I. To increase neutrophil counts in patients with myelodysplastic syndrome; J. To treat neutropenia secondary to hypersplenism". 4. **Changed Exclusion Criteria from:** "Not covered for AIDS, Hairy cell leukemia, Myelodysplasia, drug induced congenital agranulocytosis, or Alloimmune neonatal neutropenia" **to:** "Prevention of cytopenia in patients who are scheduled for, but not receiving, myelosuppressive chemotherapy; Treating chronic marrow failure (low white blood cell counts) due to prior chemotherapy treatment; To treat drug-induced neutropenias other than those causes listed above under Prior Authorization Criteria". 5. **Added** "The quantity is limited to a maximum of a 30 day supply per fill" **to Quantity/Days Supply Restrictions**. 6. **Changed Re-Authorization under Approval Length from** "Updated letter of medical necessity" **to** "An updated letter of medical necessity or progress notes showing current medical necessity criteria are met and that the medication is effective". 7. **Updated references** to include Capital Blue Cross policy, Medi-Span, and package inserts.