i. Patient is receiving myelosuppressive anti-cancer medications that are associated with a high risk of febrile neutropenia (the risk is at least 20% based on the chemotherapy regimen); OR

ii. Patient meets both of the following (a and b):

a) Patient is receiving myelosuppressive anti-cancer medications that are associated with a risk of febrile neutropenia, but the risk is less than 20% based on the chemotherapy regimen; AND

b) Patient has at least one risk factor for febrile neutropenia according to the prescriber; OR
Note: Examples of risk factors include age ≥ 65 years; prior chemotherapy or radiation therapy; persistent neutropenia; bone marrow involvement by tumor; recent surgery and/or open wounds; liver and/or renal dysfunction; poor performance status; or human immunodeficiency virus (HIV) infection.

iii. Patient meets both of the following (a and b):

a) Patient has had a neutropenic complication from prior chemotherapy and did not receive prophylaxis with a colony stimulating factor; AND
Note: Examples of colony stimulating factors include filgrastim products, pegfilgrastim products, and sargramostim products (e.g., Leukine).

b) A reduced dose or frequency of chemotherapy may compromise treatment outcome; OR

iv. Patient who has received chemotherapy has febrile neutropenia and has at least one risk factor for poor clinical outcomes or for developing infection-associated complications according to the prescriber; AND
Note: Examples of risk factors include sepsis syndrome; age > 65 years; severe neutropenia (absolute neutrophil count [ANC] < 100 cells/mm^3); neutropenia expected to be > 10 days in duration; invasive fungal infection; or other clinically documented infections.

B) The medication is prescribed by or in consultation with an oncologist or hematologist.

4. **Peripheral Blood Progenitor Cell Collection and Therapy.** Approve for 1 month if prescribed by or in consultation with an oncologist, a hematologist, or a physician who specializes in transplantation.

5. **Radiation Syndrome (Hematopoietic Syndrome of Acute Radiation Syndrome).** Approve for 1 month if prescribed by or in consultation with a physician who has expertise in treating acute radiation syndrome.

6. **Severe Chronic Neutropenia (e.g., Congenital Neutropenia, Cyclic Neutropenia, Idiopathic Neutropenia).** Approve for 6 months if prescribed by or in consultation with a hematologist.

Other Uses with Supportive Evidence

7. **Acute Lymphoblastic Leukemia.** Approve for 1 month if prescribed by or in consultation with an oncologist or a hematologist.

8. **Cytokine Release Syndrome Associated with Chimeric Antigen Receptor (CAR) T-Cell Therapy.** Approve for 1 month if prescribed for a patient who has neutropenia.
Note: Examples of CAR T-cell therapy include Kymriah (tisagenlecleucel intravenous infusion) and Yescarta (axicabtagene ciloleucel intravenous infusion).

9. **Drug-Induced (Non-Chemotherapy) Agranulocytosis or Neutropenia.** Approve for 1 month.

10. **Myelodysplastic Syndromes.** Approve for 3 months if prescribed by or in consultation with an oncologist or hematologist.

11. Neutropenia Associated with Human Immunodeficiency Virus (HIV) or Acquired Immunodeficiency Syndrome (AIDS). Approve for 4 months if the agent is prescribed by or in consultation with a physician who specializes in infectious diseases, a hematologist, or a physician who specializes in the management of HIV/AIDS.

12. Radiation-Induced Neutropenia. Approve for 6 months if the patient meets the following criteria (A and B):
- **A)** Patient is not currently receiving chemotherapy; AND
- **B)** The medication is prescribed by or in consultation with an oncologist, radiologist, or radiation oncologist.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of filgrastim products is not recommended in the following situations:

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Neupogen® subcutaneous or intravenous injection [prescribing information]. Thousand Oaks, CA: Amgen; April 2021.
2. Zarxio™ subcutaneous or intravenous injection [prescribing information]. Princeton, NJ: Sandoz; March 2021.
3. Nivestym™ subcutaneous or intravenous injection [prescribing information]. Lake Forest, IL and New York, NY: Hospira and Pfizer; August 2022.
4. Releuko® subcutaneous or intravenous injection [prescribing information]. Bridgewater, NJ: Amneal; April 2022.
5. The NCCN Acute Lymphoblastic Leukemia Clinical Practice Guidelines in Oncology (version 2.2022 – June 14, 2022). © 2022 National Comprehensive Cancer Network. Available at http://www.nccn.org. Accessed on August 16, 2022.
6. The NCCN Hematopoietic Cell Transplantation Clinical Practice Guidelines in Oncology (version 1.2022 – April 1, 2022). © 2022 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on August 16, 2022.
7. The NCCN Hematopoietic Growth Factors Clinical Practice Guidelines in Oncology (version 1.2022 – December 22, 2021). © 2021 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on August 16, 2022.
8. The NCCN Management of Immunotherapy-Related Toxicities Clinical Practice Guidelines in Oncology (version 1.2022 – February 28, 2022). © 2022 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on August 16, 2022.
9. The NCCN Myelodysplastic Syndromes Clinical Practice Guidelines in Oncology (version 3.2022 – January 13, 2022). © 2022 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed: August 16, 2022.
10. Smith TJ, Bohlke K, Lyman GH, Carson KR, et al. Recommendations for the use of WBC growth factors: American Society of Clinical Oncology Clinical Practice Guideline Update. *J Clin Oncol*. 2015;33(28):3199-3212.
11. Kuritzkes DR, Parenti D, Ward DJ, et al, and the G-CSF 930101 study group. Filgrastim prevents severe neutropenia and reduces infective morbidity in patients with advanced HIV infection: Results of a randomized, multicenter controlled trial. *AIDS*. 1998;12:65-71.
12. Hermans P, Rozenbaum W, Joy A, et al, and the G-CSF 92105 Study Group. Filgrastim to treat neutropenia and support myelosuppressive medication dosing in HIV infection. *AIDS*. 1996;10:1627-1633.
13. Kurizkes DR. Neutropenia, neutrophil dysfunction, and bacterial infection in patients with human immunodeficiency virus disease: The role of granulocyte colony-stimulating factor. *Clin Infect Dis*. 2000;30:256-260.
14. Mitsuyasu R. Prevention of bacterial infections in patients with advanced HIV infection. *AIDS*. 1999;13(Suppl 2):S19-S23.
15. Tesfa D, Keisu M, Palblad J. Idiosyncratic drug-induced agranulocytosis: Possible mechanism and management. *Am J Hematol*. 2009;84:428-434.
16. Andersohn F, Konzen C, Garbe E. Systematic review: Agranulocytosis induced by nonchemotherapy drugs. *Ann Intern Med*. 2007;146:657-665.
17. Beaushesne MF, Shalansky SJ. Nonchemotherapy drug-induced agranulocytosis: A review of 118 patients treated with colony-stimulating factors. *Pharmacother*. 1999;19(3):299-305.
18. Bhatt V, Saleem A. Review: Drug-induced neutropenia-pathophysiology, clinical features, and management. *Ann Clin Lab Sci*. 2004;34(2):131-136.
19. Curtis BR. Drug-induced immune neutropenia/agranulocytosis. *Immunohematology*. 2014;30(2):95-101.
20. Andres E, Mourot-Cottet R. Non-chemotherapy drug-induced neutropenia – an update. *Expert Opin Drug Saf*. 2017;16(11):1235-1242.

21. Andres E, Mourot-Cottet R, Maloisel F, et al. Idiosyncratic drug-induced neutropenia and agranulocytosis. *QJM*. 2017 May;110(5):299-305.