Ziextenzo™ (pegfilgrastim-bmez)

Humana

Pharmacy Coverage Policy

Effective Date: November 27, 2019
Revision Date: July 17, 2020
Review Date: June 17, 2020
Line of Business: Medicare, Commercial
Policy Type: Prior Authorization

Disclaimer

Description

Ziextenzo (pegfilgrastim-bmez) is a covalent conjugate of recombinant methionyl human G-CSF (filgrastim) and monomethoxypolyethylene glycol. Both filgrastim and Ziextenzo (pegfilgrastim-bmez) are colony stimulating factors that act on hematopoietic cells by binding to specific cell surface receptors thereby stimulating proliferation, differentiation, commitment, and end cell functional activation.

Endogenous G-CSF is a lineage specific colony-stimulating factor which is produced by monocytes, fibroblasts, and endothelial cells. G-CSF regulates the production of neutrophils within the bone marrow. G-CSF is not species specific and has been shown to have minimal direct in vivo or in vitro effects on the production of hematopoietic cell types other than the neutrophil lineage.

Ziextenzo (pegfilgrastim-bmez) is indicated for febrile neutropenia prophylaxis following the administration of myelosuppressive chemotherapy that carries a significant risk for causing febrile neutropenia.

Pegfilgrastim-bmez is available as Ziextenzo 6mg/0.6mL prefilled syringe.

Coverage Determination

Please note the following regarding medically accepted indications:

All reasonable efforts have been made to ensure consideration of medically accepted indications in this policy. Medically accepted indications are defined by CMS as those uses of a covered Part D drug that are approved under the federal Food, Drug and Cosmetic Act, or the use of which is supported by one or more citations included or approved for inclusion in any of the compendia described in section 1927(g)(1)(B)(i) of the Act. These compendia guide review of off-label and off-evidence prescribing and are subject to minimum evidence standards for each compendium. Currently, this review includes the following references when applicable and may be subject to change per CMS:

- American Hospital Formulary Service-Drug Information (AHFS-DI)
- National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium
- Truven Health Analytics Micromedex DrugDEX
- Elsevier/Gold Standard Clinical Pharmacology
- Wolters Kluwer Lexi-Drugs

Ziextenzo (pegfilgrastim-bmez) will require prior authorization. This agent may be considered medically necessary when the following criteria are met:

Febrile Neutropenia Prophylaxis

- The member must have a diagnosis of non-myeloid malignancy (e.g.breast cancer, lung cancer) **AND**
- The member has received or will receive myelosuppressive chemotherapy during the 24-72 hour time frame prior to pegfilgrastim injection **AND**
- The member must also meet ONE OR MORE of the following criteria:
  - 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) **OR**
  - A risk of febrile neutropenia of 10-20% based on chemotherapy regimen, and one or more of the following risk factors apply:

- Prior chemotherapy or radiation therapy
- 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)
- Bone marrow involvement by tumor
- Recent surgery and/or open wounds
- Liver dysfunction (bilirubin greater than 2.0 mg/dL)
- Renal dysfunction (creatinine clearance less than 50 mL/min)
- Age greater than 65 receiving full chemotherapy dose intensity **OR**

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

Recommended Treatment:

- The recommended dosage of Ziextenzo (pegfilgrastim-bmez) is a single subcutaneous injection of 6 mg administered once per chemotherapy cycle.
- Ziextenzo (pegfilgrastim-bmez) should not be administered concomitantly (on the same day) with myelosuppressive chemotherapy.
- Ziextenzo (pegfilgrastim-bmez) should be administered ~24-72 hours following myelosupressive chemotherapy and the member should not receive additional chemotherapy for a period of 14 days followingZiextenzo (pegfilgrastim-bmez) administration.
- Ziextenzo (pegfilgrastim-bmez) should not be utilized in myelosuppressive chemotherapy regimens that are administered more frequently than every two weeks.

Pegfilgrastim therapy will be approved for 120-day intervals.

The quantity limit for pegfilgrastim is two (6 mg) syringes per 28 days.

Coverage Limitations

Ziextenzo (pegfilgrastim-bmez) therapy is not considered medically necessary in members with the following concomitant conditions:

- Concomitant use (within seven days of Ziextenzo (pegfilgrastim-bmez) dose) with filgrastim, biosimilar filgrastim (e.g. filgrastim-sndz or filgrastim-aafi), tbo-filgrastim or sargramostim
- Same day administration with myelosuppressive chemotherapy or therapeutic radiation
- Cannot be given more than once per chemotherapy cycle and cannot be given more often than every 14 days (cannot be utilized in myelosuppressive chemotherapy regimens that are administered more frequently than every two weeks)
- Experimental/Investigational Use – Indications not supported by CMS recognized compendia or acceptable peer reviewed literature.

Background

This is a prior authorization policy about Ziextenzo (pegfilgrastim-bmez).

The prophylactic use of colony-stimulating factors (CSFs) can reduce the risk, severity, and duration of both severe neutropenia and febrile neutropenia. Despite these benefits, CSFs are not administered to all patients receiving myelosuppressive chemotherapy because of the costs associated with their routine use. The selective use of CSFs in patients at increased risk for neutropenic complications may, however, enhance their cost-effective use by directing treatment toward those members who are most likely to benefit.

The preventative use of CSF reduces the incidence, length and severity of chemotherapy-

related neutropenia and may prevent life-threatening complications. The definition of members at high risk for severe or febrile neutropenia is outlined in ASCO guidelines referenced in this document.

Guidelines do not recommend the same day administration of chemotherapy with either Neulasta (pegfilgrastim) or any myeloid growth factor. While there is no argument that this is more convenient, safety is a real concern and supporting data is still conflicting. The NCCN Myeloid Growth Factor Guidelines (V1.2012) and the ASCO 2006 myeloid growth factor guidelines do not recommend same day administration of myeloid growth factors and myelosuppressive chemotherapy. Randomized phase II trials of Neulasta (pegfilgrastim) administration the same day as chemotherapy versus administration the day after chemotherapy have shown less benefit in two studies of regimens associated with moderate to high risk neutropenia, and comparable benefit in one study of a regimen with low risk neutropenia where pegfilgrastim would not routinely be indicated. Therefore (per NCCN) same day administration is not recommended.

Per NCCN: There are insufficient data to support dose and schedule of weekly regimens or chemotherapy schedules less than two weeks and these cannot be recommended.

Ziextenzo (pegfilgrastim-bmez) should not be used in the following:

- Should not be used in infants, children, and smaller adolescents weighing less than 45 kg—pegfilgrastim is not FDA approved for pediatric use
- Routine use as prophylaxis in members/chemotherapy regimens without significant risk of febrile neutropenia or in members that are not receiving myelosuppressive chemotherapy
- Partial doses (utilizing a portion of the 6mg dose for multiple or partial doses)
- Treatment of neutropenia or febrile neutropenia (only approved for prophylaxis)

- See also Coverage Limitations section of policy.

Provider Claims Codes

All provider claims codes surrounding this topic may not be included in the following table:

CPT© Codes	Description	Comments
96372	Therapeutic, prophylactic, or diagnostic injection (specify substance or drug); subcutaneous or intramuscular	

HCPC© Codes	Description	Comments
Q5120	Injection, pegfilgrastim-bmez, biosimilar, (ziextenzo), 0.5 mg	Effective 7/01/2020

Medical Terms

Ziextenzo; pegfilgrastim-bmez; prophylaxis febrile neutropenia; myeloid growth factor; subcutaneous; pharmacy

References

AHFS Drug Information. American Society of Health-System Pharmacists, Inc. Bethesda, MD 2020.

Berghmans T, Paesmans M, Lafitte JJ, et al. Therapeutic use of granulocyte and granulocyte-macrophage colony-stimulating factors in febrile neutropenic cancer patients: A systematic review of the literature with meta-analysis. *Support Care Cancer* 10:181-188. 2002.

Beyer J, Schwella N, Zingsem J, et al. Hematopoietic rescue after high-dose chemotherapy using autologous peripheral-blood progenitor cells or bone marrow: a randomized comparison. *J Clin Oncol.* 1995; 13:1328-1335.

Citron ML, Berry DA, Cirrincione C, et al. Randomized trial of dose-dense versus conventionally scheduled and sequential versus concurrent combination chemotherapy as postoperative adjuvant treatment of node-positive primary breast cancer: First report of Intergroup Trial C9741/Cancer and Leukemia Group B Trial 9741. *J Clin Oncol* 21:1431-1439. 2003.

Dale DC, Bonilla MA, Davis MW, et al. A randomized controlled phase III trial of recombinant human granulocyte colony-stimulating factor (filgrastim) for treatment of severe chronic neutropenia. *Blood* 81(10):2496-502. 1993.

Dubois RW, Pinto LA, Bernal M, et al. Benefits of GM-CSF versus placebo or G-CSF in reducing chemotherapy-induced complications: A systematic review of the literature. *Support Cancer Therapy* 2:34-41, 2004.

Ganser A, Volkers B, Greher J, et al. Recombinant human granulocyte-macrophage colony-stimulating factor in members with myelodysplastic syndromes – a phase I/II trial. *Blood* 73(1):31-7.1989.

Garavelli PJ, Berti P. Efficacy of recombinant granulocyte colony-stimulating factor in the long-term treatment of AIDS-related neutropenia. *AIDS*. 7(4):589-90. 1993.

Garcia-Carbonero R, Mayordomo JI, Tornamira MV, et al. Granulocyte colony-stimulating factor in the treatment of high-risk febrile neutropenia: A multi-center randomized trial. *J Natl Cancer Inst* 93:31-38. 2001.

Green MD, Koelbl H, Baselga J et al. A randomized double-blind multicenter phase III study of fixed-dose single-administration pegfilgrastim versus daily filgrastim in members receiving myelosuppressive chemotherapy. *Ann Oncol* 2003; 14: 29–35.

Heath JA, Steinherz PG, Altman A, et al. Human granulocyte colony-stimulating factor in children with high-risk acute lymphoblastic leukemia: A Children's Cancer Group Study. *J Clin Oncol* 21:1612-1617. 2003.

Hermans P, Rozenbaum W, Jou A, et al. Filgrastim to treat neutropenia and support myelosuppressive medication dosing in HIV infection. G-CSF 92105 Study Group. *AIDS* 10(14):1627-33. 1996.

Heil G, Hoeizer D, Sanz MA, et al. The International Acute Myeloid Leukemia Study Group. A randomized, double-blind, placebo-controlled, phase III study of filgrastim in

remission induction and consolidation therapy for adults with de novo acute myeloid leukemia – The International Acute Myeloid Leukemia Study Group. *Blood* 90:4710-4718. 1997.

Holmes FA, O'Shaughnessy J, Vukelja S et al. Blinded, randomized, multicenter study to evaluate single administration pegfilgrastim once per cycle versus daily filgrastim as an adjunct to chemotherapy in patients with high-risk stage II or stage III/IV breast cancer. *J Clin Oncol* 2002; 20: 727–731.

Hughes WT, Armstrong D, Bodey GP, et al. 2002 guidelines for the use of antimicrobial agents in neutropenic patients with cancer. *Clin Infect Dis* 34(6):730-51. 2002.

Kroger N, Zander AR. Dose and schedule effect of G-CSF for stem cell mobilization in healthy donors for allogeneic transplantation. *Leuk Lymphoma*. 43:1391-1394. 2002.

Lexicomp Online® , Hudson, Ohio: Lexi-Comp, Inc. 2020.

Lyman GH, Kuderer NM. Epidemiology of febrile neutropenia. *Support Cancer Therapy.* 1:23-35. 2003.

Micromedex Healthcare Series: Thomson Micromedex, Greenwood Village, Colorado. 2020.

National Comperhensive Cancer Network (NCCN). Clinical Practice Guidelines in Oncology: Myeloid Growth Factors. 2020.

Nemunaitis J, Rabinowe SN, Singer JW, et al. Recombinant granulocyte-macrophage colony-stimulating factor after autologous bone marrow transplantation for lymphoid cancer. *N Engl J Med* 324(25):1773-8. 1991.

Nemunaitis J, Rosenfeld CS, Ash R, et al. Phase III randomized, double-blind, placebo-controlled trial of rhGM-CSF following allogeneic bone marrow transplantation. *Bone Marrow Transplant.* 15(6):949-54. 1995.

Nemunaitis J, Singer JW, Buckner CD, et al. Use of recombinant human granulocyte-macrophage colony-stimulating factor in graft failure after bone marrow transplantation. *Blood.* 76(1):245-53. 1990.

Neulasta Prescribing Information. Amgen, Inc.; Thousand Oaks, CA: January 2020.

Pfeundschuh M, Truemper L, Kloess M, et al. 2-weekly or 3-weekly CHOP chemotherapy with or without etoposide for the treatment of elderly patients with aggressive lymphomas: Results of the NHL-B2 trial of the DSHNHL. *Blood*. 104:634-641. 2004.

Ringden O, Labopin M, Gorin NC, et al. Treatment with granulocyte colony-stimulating factor after allogeneic bone marrow transplant for acute leukemia increases the risk of graft versus host disease and death: a study from the Acute Leukemia Working Party of the European Group for Blood and Marrow Transplantation. *J Clin Oncol* 22(3):416-23. 2004.

Smith T, Khatcheressian J, Lyman GH, et al. 2006 Update of Recommendations for the Use of White Blood Cell Growth Factors: An Evidence-Based Clinical Practice Guideline. *J Clin Onc* 24(19): 1- 19. Jul. 2006.

Thatcher N, Girling DJ, Hopwood P, et al. Improving survival without reducing quality of life in small-cell lung cancer members by increasing the dose-intensity of chemotherapy with granulocyte-colony-stimulating factor support: Results of a British Medical Research Council Multicenter Randomized Trial – Medical Research Council Lung Cancer Working Party. *J Clin Oncol* 18:395-404. 18:395-404. 2000

Waselenko JK, MacVittie TJ, Blakely WF, et al. Medical management of acute radiation syndrome. Recommendations of the Strategic National Stockpile Radiation Working Group. *Ann Intern Med* 140(12):1037-51. 2004.

Ziextenzo Prescribing Information. Sandoz; Princeton, NJ. November 2019.