

PROPRIETARY & CONFIDENTIAL

POLICY NUMBER UM ONC_1072	SUBJECT Myeloid Growth Factors Neupogen (Filgrastim), Granix (tbo-filgrastim), Sargramostim (Leukine), Zarxio (filgrastim-sndz), Nivestym (filgrastim-aafi), Neulasta/Neulasta Onpro Kit (pegfilgrastim) Kit, Fulphila (pegfilgrastim-jmdb), Udenyca (pegfilgrastim-cbqv) and Ziextenzo (pegfilgrastim-bmez)		DEPT/PROGRAM UM Dept	PAGE 1 OF 4
DATES COMMITTEE REVIEWED 02/23/11, 03/08/12, 07/10/13, 04/09/14, 09/10/14, 10/14/15, 07/26/16, 03/08/17, 06/14/17, 06/13/18, 09/12/18, 10/10/18, 01/09/19, 07/10/19, 09/11/19, 12/11/19, 01/08/20, 02/12/20, 03/11/20, 04/08/20, 05/13/20	APPROVAL DATE May 13, 2020	EFFECTIVE DATE May 29, 2020	COMMITTEE APPROVAL DATES (latest version listed last) 02/23/11, 03/08/12, 07/10/13, 04/09/14, 09/10/14, 10/14/15, 07/26/16, 03/08/17, 06/14/17, 06/13/18, 09/12/18, 10/10/18, 01/09/19, 07/10/19, 09/11/19, 12/11/19, 01/08/20, 02/12/20, 03/11/20, 04/08/20, 05/13/20	
PRIMARY BUSINESS OWNER: UM APPROVED BY: Dr. Andrew Hertler		COMMITTEE/BOARD APPROVAL Utilization Management Committee		
URAC STANDARDS HUM 1		NCQA STANDARDS UM 2		ADDITIONAL AREAS OF IMPACT
CMS REQUIREMENTS	STATE/FEDERAL REQUIREMENTS		APPLICABLE LINES OF BUSINESS All	

I. PURPOSE

To define and describe the accepted indications for Myeloid Growth Factors Neupogen (Filgrastim), Granix (tbo-filgrastim), Sargramostim (Leukine), Zarxio (filgrastim-sndz), Nivestym (filgrastim-aafi), Neulasta/Neulasta Onpro Kit (pegfilgrastim) Kit, Fulphila (pegfilgrastim-jmdb), Udenyca (pegfilgrastim-cbqv) and Ziextenzo (pegfilgrastim-bmez) in the treatment of cancer, including FDA approved indications, and off-label indications.

New Century is responsible for processing all medication requests from network ordering providers. Medications not authorized by New Century may be deemed as not approvable and therefore not reimbursable.

The use of this drug must be supported by one of the following: FDA approved product labeling, CMS-approved compendia, National Comprehensive Cancer Network (NCCN), American Society of Clinical Oncology (ASCO) clinical guidelines, or peer-reviewed literature that meets the requirements of the CMS Medicare Benefit Policy Manual Chapter 15.

II. INDICATIONS FOR USE/INCLUSION CRITERIA

1. PREFERRED MEDICATION GUIDANCE FOR INITIAL REQUEST:

- When health plan Medicaid coverage provisions- including any applicable PDLs (Preferred Drug Lists)- conflict with the coverage provisions in this drug policy, health plan Medicaid coverage provisions take precedence per the **Preferred Drug Guidelines OR**
- When health plan Exchange coverage provisions- including any applicable PDLs (Preferred Drug Lists)- conflict with the coverage provisions in this drug policy, health plan Exchange coverage provisions take precedence per the **Preferred Drug Guidelines OR**
- For Health Plans that utilize NCH UM Oncology Clinical Policies as the initial clinical criteria, the **Preferred Drug Guidelines shall follow NCH L1 Pathways** when applicable, otherwise shall follow NCH drug policies **AND**
- Continuation requests of previously approved non-preferred medication are not subject to this provision.
- When available, generic alternatives are preferred over brand-name drugs **AND**
- Fulphila (pegfilgrastim-jmdb) OR Ziextenzo (pegfilgrastim-bmez) are the **PREFERRED** medications whenever a long acting myeloid growth factor (pegfilgrastim) is requested **AND**



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- g. Zarxio (filgrastim-sndz) is the **PREFERRED** medication whenever a short acting myeloid growth factor (filgrastim) is requested **AND**
- h. Non-preferred myeloid growth factor agent will be approved only if there is a contraindication/intolerance to the **PREFERRED** medication.

2. Prophylaxis/Prevention of Febrile Neutropenia from Chemotherapy

- a. NOTE: Short-acting growth factors are preferred, over long acting, when a limited number of doses (generally less than 10) are required/clinically indicated. Long acting growth factors are appropriate, per NCH policy, if the member is unable to self-inject or if the need for daily travel- to receive multiple (generally 10 doses) daily injections of a short acting growth factor- would cause undue hardship to the member.
- b. The member has a solid tumor or non-myeloid malignancy and is receiving MGF for any of the following:
 - i. MGF is being used for chemotherapy with high-risk (greater than 20%) for febrile neutropenia **OR**
 - ii. MGF is being used with chemotherapy with an intermediate-risk (10% to 20%) for febrile neutropenia **AND** the member has **ONE** or more of the following risk factors:
 - A. Age \geq 65 years; extensive prior chemotherapy or radiation therapy; persistent/pre-existing neutropenia; bone marrow involvement by tumor; recent surgery and/or open wounds; liver dysfunction (bili > 2.0), or renal dysfunction (crcl < 50).

3. Myelodysplastic Syndromes (MDS)

- a. A short acting MGF (NCH Preferred is Zarxio) is being used in combination with lenalidomide and/or epoetin or darbepoetin alpha in members with no response to erythropoietin alone **OR**
- b. The member has MDS and a short acting MGF (NCH Preferred is Zarxio) is being used for neutropenia **AND** prevention of infections.

4. Treatment of Febrile Neutropenia

- a. Member has documented febrile neutropenia as defined by the Infectious Disease Society of America as: An ANC (Absolute Neutrophil Count) of <1.0 (1000 cells/micoL) **AND** a single oral temperature of \geq 38.3 degree C (101 degree F) or a temperature of \geq 38.0 degree C (100.4 degree F) sustained over a 1 hour period **AND**
- b. A short acting MGF (NCH Preferred is Zarxio) is being used with appropriate antibiotic therapy.

III. EXCLUSION CRITERIA

- 1. MGF use for primary prophylaxis of febrile neutropenia in members who are receiving chemotherapy that has a low risk for febrile neutropenia.
- 2. MGF use for the treatment of afebrile neutropenia.
- 3. Member is not receiving myelosuppressive chemotherapy for non-myeloid malignancy or solid tumor.
- 4. Pegfilgrastim use with weekly myelosuppressive chemotherapy regimens (Neupogen, Leukine, Zarxio, Nivestym, or Granix should be used in these circumstances).
- 5. Neupogen, Leukine, Zarxio, Nivestym, or Granix use within 7 days of Pegfilgrastim.
- 6. Pegfilgrastim use in myeloid malignancies or MDS.
- 7. Indications not supported by CMS recognized compendia or acceptable peer reviewed literature.



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IV. MEDICATION MANAGEMENT

Please refer to the FDA label/package insert for details regarding these topics.

V. APPROVAL AUTHORITY

1. Review – Utilization Management Department
2. Final Approval – Utilization Management Committee

VI. ATTACHMENTS

None

VII. REFERENCES

1. Brusamolino E, et al. Haematologica, Volume 91, Issue 4 April dated 2006, Pgs. 496-502. Dose-dense R-CHOP-14 supported by pegfilgrastim in patients with diffuse large B-cell lymphoma: a phase II study of feasibility and toxicity.
2. Burstein HJ, et al. Journal of Clinical Oncology, Volume 23, Issue 33 dated November 20, 2005, Pgs. 8340-7. Efficacy of pegfilgrastim and darbepoetin alfa as hematopoietic support for dose-dense every-2-week adjuvant breast cancer chemotherapy.
3. Jones RL, et al. British Journal of Cancer, Volume 100, Issue 2 dated January 27, 2009, Pgs. 305-10. A randomized pilot Phase II study of doxorubicin and cyclophosphamide (AC) or epirubicin and cyclophosphamide (EC) given 2 weekly with pegfilgrastim (accelerated) vs 3 weekly (standard) for women with early breast cancer
4. Hecht JR, et al. Clinical Colorectal Cancer, Volume 9, Issue 2 dated April 2010, Pgs. 95-101. A randomized, placebo-controlled phase ii study evaluating the reduction of neutropenia and febrile neutropenia in patients with colorectal cancer receiving pegfilgrastim with every-2-week chemotherapy.
5. 2006 Update of Recommendations for the Use of White Blood Cell Growth Factors: An Evidence-Based Clinical Practice Guideline. Smith T et al. JCO 24:1-19, 2006.
6. ASCO's position on same day dosing accessed on 9/4/14:
<http://www.wsmos.org/assets/Letter%20to%20CMS%20RAC%20Audit%20on%20Neulasta%20110912%20lthd.pdf>
7. NCCN Practice Guidelines in Oncology: Myeloid Growth Factors. November, 2020.
8. Zarxio prescribing information. Sandoz Inc. Princeton, NJ. 2018.
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10. Neupogen prescribing information. Amgen, Inc. Thousand Oaks, California. 2018.
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13. Fulphila prescribing information. Mylan Institutional LLC, Rockford, IL 2019.
14. Nivestym prescribing information. Pfizer Laboratories Div Pfizer Inc New York, NY 2019.
15. Udenyca prescribing information. Coherus BioSciences, Inc., Redwood City, California 2019.
16. Ziextenzo prescribing information. Sandoz Inc. Princeton, NJ. 2019.
17. Clinical Pharmacology Elsevier Gold Standard. 2020.
18. Micromedex® Healthcare Series: Thomson Micromedex, Greenwood Village, Co. 2020.
19. National Comprehensive Cancer Network. Cancer Guidelines and Drugs and Biologics Compendium. 2020.



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20. AHFS Drug Information. American Society of Health-Systems Pharmacists or Wolters Kluwer Lexi-Drugs. Bethesda, MD. 2020.

VIII. ADDENDUM

1. **Preferred product(s) for Arizona Health Care Cost Containment System (AHCCCS), Arizona's Medicaid agency: Neupogen/Udenyca/Fulphila**

For AHCCCS members: when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy for a list of NON-preferred products.