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Drug Class Literature Scan: Colony Stimulating Factors

Date of Review: June 2021

Date of Last Review: January 2019
Literature Search: 09/01/18 – 03/25/21

Current Status of PDL Class:
See **Appendix 1**.

Conclusions:

- There is limited new evidence available for evaluation of this class. No high-quality systematic reviews met inclusion criteria for review, many of which include biosimilar products not approved for use in the United States. One guideline was included in this review. Evidence supports previous recommendations with no compelling new evidence of efficacy or harms between granulocyte-colony stimulating factors (G-CSF), including between reference products and biosimilar formulations.
- Prophylaxis of febrile neutropenia (FN): evidence supports use with no differentiation between filgrastim, filgrastim biosimilars, tbo-filgrastim, pegfilgrastim, or pegfilgrastim biosimilars.[1]
- Treatment of FN: evidence supports use of filgrastim, filgrastim biosimilars, tbo-filgrastim, and sargramostim for FN due to chemotherapy; all reference and biosimilar G-CSF products and sargramostim (a granulocyte macrophage colony stimulating factor [GM-CSF]) are recommended for hematopoietic acute radiation syndrome (H-ARS).[1] (Note: Biosimilar products and tbo-filgrastim do not carry H-ARS as an official Food and Drug Administration (FDA) indication [**Appendix 6**]).
- Mobilization of Progenitor Cells:
    - Autologous Setting: evidence supports filgrastim, filgrastim biosimilars, and tbo-filgrastim; there is a lower rated recommendation for concurrent filgrastim or filgrastim biosimilars in combination with sargramostim.
    - Allogeneic Donors: evidence supports filgrastim and filgrastim biosimilars as the preferred choice, with tbo-filgrastim as an additional option.
    - Post-Hematopoietic Cell Transplant Supportive Care: evidence supports all G-CSF products.[1]
- Pegfilgrastim-apgf (Nyvepria™) was approved in June 2020 as a biosimilar to pegfilgrastim (Neulasta®) for all indications except H-ARS (**Appendix 6**).[2]
- Multiple new FDA safety alerts and package labeling changes have been enacted since the previous review (**Table 2**).

Recommendations:

- No changes to the Oregon Health Plan Preferred Drug List (PDL) were made based on clinical evidence.
- Nyvepria (pegfilgrastim-apgf) was made preferred and Neulasta (pegfilgrastim) products were made non-preferred after evaluation of comparative costs in executive session.

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Summary of Prior Reviews and Current Policy

- Most recent update of class occurred in January 2019, where tbo-filgrastim was reviewed and added as a preferred product. Currently all reference products are preferred on the PDL, while biosimilar products remain non-preferred. There are no class specific prior authorization criteria beyond preferred vs. non-preferred status.
- Previous evidence summaries concluded no compelling evidence of efficacy or harms differences between G-CSF products. Evidence is generally of moderate quality for FN prophylaxis, FN treatment, and hematopoietic progenitor cell transplant.
- Overall class usage is relatively low with fewer than 10 patients in the fee-for-service only population.

Methods:

A Medline literature search for new systematic reviews and randomized controlled trials (RCTs) assessing clinically relevant outcomes to active controls, or placebo if needed, was conducted. A summary of the clinical trials is available in **Appendix 2** with abstracts presented in **Appendix 3**. The Medline search strategy used for this literature scan is available in **Appendix 4**, which includes dates, search terms and limits used. The OHSU Drug Effectiveness Review Project, Agency for Healthcare Research and Quality (AHRQ), National Institute for Health and Clinical Excellence (NICE), Department of Veterans Affairs, and the Canadian Agency for Drugs and Technologies in Health (CADTH) resources were manually searched for high quality and relevant systematic reviews. When necessary, systematic reviews are critically appraised for quality using the AMSTAR tool and clinical practice guidelines using the AGREE tool. The FDA website was searched for new drug approvals, indications, and pertinent safety alerts.

The primary focus of the evidence is on high quality systematic reviews and evidence-based guidelines. Randomized controlled trials will be emphasized if evidence is lacking or insufficient from those preferred sources.

New Systematic Reviews:

After review, 11 systematic reviews were excluded due to poor quality, wrong study design of included trials (e.g., observational), comparator (e.g., no control, placebo-controlled, or non-FDA approved product included), or outcome studied (e.g., non-clinical).[3-13]

New Guidelines:

National Comprehensive Cancer Network-Myeloid Growth Factors

The NCCN issued updated guidelines in March of 2021 (version 2.2021) on the use of hematopoietic growth factors.[1] Methods for NCCN guideline development are published. Panel members with meaningful conflicts of interest (COI) are excluded from panel presentations, reviews, discussions, and voting in areas relevant to the COI. Active guidelines are reviewed and updated at least annually. NCCN categories for recommendations are based on level of clinical evidence and degree of consensus within the guideline panel related to both efficacy and safety. **(Table 1)** The level of evidence is based on quality of data, quantity of data, and consistency of data. This guideline review panel had fewer than half of the members with significant COI. These guidelines were developed specifically for adult patients. All recommendations are category 2A unless otherwise noted.

Table 1. NCCN Categories of Evidence and Consensus[1]

Category	Description
1	Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate

2A	Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate
2B	Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate
3	Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate
All recommendations are 2A unless otherwise indicated	

Febrile Neutropenia Prophylaxis

Use of G-CSF for prophylaxis of FN in patients with solid tumors and non-myeloid malignancies is stratified by risk. This risk is dependent on multiple factors including diagnosis, chemotherapy regimen, patient risk factors, and treatment goals. G-CSF are recommended in patients with high risk of FN (>20%) (category 1). Intermediate risk patients (10-20%) may be considered for G-CSF treatment with the presence of any risk factors (e.g. bone marrow involvement of tumor, recent surgery, liver dysfunction, etc). G-CSF prophylaxis is not recommended in those with low risk (<10%). Additionally, use of G-CSF should be considered in patients who develop febrile neutropenia or a dose limiting neutropenic event who did not receive G-CSF during the prior chemotherapy cycle. Filgrastim, tbo-filgrastim, and pegfilgrastim are all recommended (category 1), and FDA-approved biosimilars are considered appropriate substitutes for filgrastim and pegfilgrastim.[1]

Febrile Neutropenia Treatment

For a patient who develops FN, G-CSF use is dependent on previous exposure and agent used. Patients who received FN prophylaxis with a long acting product (e.g., pegfilgrastim or biosimilar) should not receive additional G-CSF. Pharmacokinetic data suggest it may not be beneficial to give additional G-CSF to a patient who received a long-acting product, though in prolonged neutropenia it may be considered. Patients who received prophylaxis with a short acting product (e.g., filgrastim or biosimilars, tbo-filgrastim) should continue therapy until absolute neutrophil count (ANC) recovery.[1]

Patients who develop FN, did not receive G-CSF prophylaxis, and do not have risk factors for an infection associated complication (e.g., sepsis syndrome, age greater than 65 years, ANC less than 100/mcL, neutropenia duration expected to be greater than 10 days, etc.) should not receive G-CSF or GM-CSF. Patients with risk factors may consider therapeutic use of short-acting G-CSF or GM-CSF until post-nadir ANC recovers to normal or near normal levels. Therapeutic use of G-CSF or GM-CSF should be used for radiation-induced myelosuppression following a radiologic or nuclear incident (H-ARS).[1]

Mobilization of Hematopoietic Progenitor Cells in Autologous Setting

Myeloid growth factors mobilization has multiple recommended regimens. Filgrastim (or biosimilars) or tbo-filgrastim administered via single or twice daily injections may be used as a single agent regimen. Use of these after combination chemotherapy, with the goal of mobilization during count recovery, may increase collection yields with fewer days of apheresis and reduce burden of residual tumor, but may also increase hospitalizations for neutropenic fever. Filgrastim (or biosimilars) plus sargramostim is an additional approach (category 2B). Filgrastim (or biosimilars) or tbo-filgrastim may also be combined with plerixafor for patients who do not mount a sufficient CD34+ count.[1]

Mobilization of Allogeneic Donors

Allogenic hematopoietic cell donors may receive either filgrastim (or biosimilars) or tbo-filgrastim (category 2B), with plerixafor (category 2B). For granulocyte transfusion, filgrastim (or biosimilars) or tbo-filgrastim (category 2B), as a single dose with dexamethasone, are recommended 8 to 24 hours prior to collection.[1]

Supportive Care Options
Filgrastim (or biosimilars) or tbo-filgrastim may be used for post-autologous hematopoietic cell transplant, haploidentical transplant, or cord blood transplant. Filgrastim is known to accelerate neutrophil recovery, though it has not been shown to impact survival. Additionally, pegfilgrastim (or biosimilars) can be considered for post-autologous hematopoietic cell transplant.[1]

After review, 3 guidelines were excluded due to poor quality or lack of applicability.[14-16]

New Formulations:
Pegfilgrastim-apgf (Nyvepria™) was approved in June 2020 as a biosimilar to pegfilgrastim (Neulasta®) and is indicated to decrease the incidence of infection, as manifested by febrile neutropenia, in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a clinically significant incidence of febrile neutropenia.

New FDA Safety Alerts:

Table 2. Description of New FDA Safety Alerts

Generic Name	Brand Name	Month / Year of Change	Location of Change (Boxed Warning, Warnings, Contraindications)	Addition or Change and Mitigation Principles (if applicable)
TBO-Filgrastim[17]	Granix®	Feb 2019	Warnings and Precautions	New subsection describing risk of alveolar hemorrhage. Hemoptysis resolved with discontinuation. Use for peripheral blood progenitor cell mobilization in healthy donors is not an approved indication.
Pegfilgrastim-jmdb[18]	Fulphila®	Mar 2019	Warnings and Precautions	Addition of aortitis Addition of nuclear imaging (hematopoietic activity is associated with transient positive bone imaging changes) Addition of thrombocytopenia Addition of myelodysplastic syndrome and acute myeloid leukemia in patients with breast and lung cancer
Filgrastim-sndz[19]	Zarxio®	Aug 2019	Warnings and Precautions	Addition of aortitis
Pegfilgrastim-bmez[20]	Ziextenzo®	Mar 2021	Warnings and Precautions	Addition of myelodysplastic syndrome and acute myeloid leukemia in patients with breast and lung cancer Addition of thrombocytopenia

References:

1. National Comprehensive Cancer Network. (March 23, 2021). Hematopoietic Growth Factors (Versin 2.2021). https://www.nccn.org/professionals/physician_gls/pdf/growthfactors.pdf. Accessed March 26, 2021. .
2. Nyvepria (pegfilgrastim-apgf) Prescribing Information. Pfizer. New York, NY. Apr 2021.
3. Cornes P, Gascon P, Chan S, et al. Systematic Review and Meta-analysis of Short- versus Long-Acting Granulocyte Colony-Stimulating Factors for Reduction of Chemotherapy-Induced Febrile Neutropenia. *Advances in Therapy.* 2018;35(11):1816-1829.
4. Yang J, Yu S, Yang Z, et al. Efficacy and Safety of Supportive Care Biosimilars Among Cancer Patients: A Systematic Review and Meta-Analysis. *Biodrugs.* 2019;33(4):373-389.
5. Botteri E, Krendyukov A, Curigliano G. Comparing granulocyte colony-stimulating factor filgrastim and pegfilgrastim to its biosimilars in terms of efficacy and safety: A meta-analysis of randomised clinical trials in breast cancer patients. *Eur J Cancer.* 2018;89:49-55.
6. Danova M, Pronzato P, Ingrasciotta Y, et al. Recent advances in the management of chemotherapy-induced neutropenia: biosimilar granulocyte colony-stimulating factor use in Italy. *Future Oncology.* 2020;16(14):891-897.
7. Bongiovanni A, Recine F, Fausti V, et al. Clinical role of filgrastim in the management of patients at risk of prolonged severe neutropenia: An evidence-based review. *International Journal of Clinical Practice.* 2019;73(11):e13404.
8. Fernandes R, Mazzarello S, Stober C, et al. Primary Febrile Neutropenia Prophylaxis for Patients Who Receive FEC-D Chemotherapy for Breast Cancer: A Systematic Review. *Journal of Global Oncology.* 2018;4:1-8.
9. Bond TC, Szabo E, Gabriel S, et al. Meta-analysis and indirect treatment comparison of lipegfilgrastim with pegfilgrastim and filgrastim for the reduction of chemotherapy-induced neutropenia-related events. *Journal of Oncology Pharmacy Practice.* 2018;24(6):412-423.
10. Wang Y, Chen L, Liu F, et al. Efficacy and tolerability of granulocyte colony-stimulating factors in cancer patients after chemotherapy: A systematic review and Bayesian network meta-analysis. *Scientific Reports.* 2019;9(1):15374.
11. Ranna V, Cheng KKF, Castillo DA, et al. Development of the MASCC/ISOO clinical practice guidelines for mucositis: an overview of the methods. *Support Care Cancer.* 2019;27(10):3933-3948.
12. Dale DC, Crawford J, Klippel Z, et al. A systematic literature review of the efficacy, effectiveness, and safety of filgrastim. *Supportive Care in Cancer.* 2018;26(1):7-20.
13. Logan RM, Al-Azri AR, Bossi P, et al. Systematic review of growth factors and cytokines for the management of oral mucositis in cancer patients and clinical practice guidelines. *Supportive Care in Cancer.* 2020;28(5):2485-2498.
14. National Comprehensive Cancer Network. NCCN Hematopoietic Growth Factors: Short-Term Recommendations Specific to Issues with Covid-19 (SARS-CoV-2). https://www.nccn.org/covid-19/pdf/HGF_COVID-19.pdf Accessed March 29, 2021.
15. Taplitz RA, EB K, EJ B, et al. Outpatient Management of Fever and Neutropenia in Adults Treated for Malignancy: American Society of Clinical Oncology and Infectious Diseases Society ofAmerica Clinical Practice Guideline Update. *J Clin Oncol* 2018(36):1443-1453.
16. Klastersky J, de Naurois J, Rolston K, et al. Management of febrile neutropaenia: ESMO Clinical Practice Guidelines. *Ann Oncol.* 2016;27(suppl 5):v111-v118.
17. Granix (tbo-filgrastim) Prescribing Information. Teva Pharmaceuticals. North Wales, PA. Mar 2019.
18. Fulphila (pegfilgrastim-jmdb) Prescribing Information. Mylan Pharmaceuticals. Morgantown, WV. Mar 2021.
19. Zarxio (filgrastim-sndz) Prescribing Information. Sandoz. Princeton, NJ. Aug 2019.
20. Ziextenzo (pegfilgrastim-bmez) Prescribing Information. Sandoz. Princeton, NJ. Mar 2021.

21. Waller CF, Ranganna GM, Pennella EJ, et al. Randomized phase 3 efficacy and safety trial of proposed pegfilgrastim biosimilar MYL-1401H in the prophylactic treatment of chemotherapy-induced neutropenia. *Annals of Hematology.* 2019;98(5):1217-1224.
22. Neupogen (filgrastim) Prescribing Information. Amgen, Inc. Thousand Oaks, Ca. Feb 2021.
23. Nivestym (filgrastim-aafi) Prescribing Information. Pfizer. Lake Forest, IL. Jul 2018.
24. Leukine (sargramostim) Prescribing Information. Sanofi. Bridgewater, NJ. Mar 2018.
25. Neulasta (pegfilgrastim) Prescribing Information. Amgen. Thousand Oaks, CA. Feb 2021.
26. Udenyca (pegfilgrastim-cbqv) Prescribing Information. Coherus Biosciences. Redwood City, CA. Sep 2019.

Appendix 1: Current Preferred Drug List

Generic	Brand	Form	Route	PDL
filgrastim	NEUPOGEN	SYRINGE	IJ	Y
filgrastim	NEUPOGEN	VIAL	IJ	Y
pegfilgrastim	NEULASTA ONPRO	SYR W/ INJ	SQ	Y
pegfilgrastim	NEULASTA	SYRINGE	SQ	Y
sargramostim	LEUKINE	VIAL	IJ	Y
tbo-filgrastim	GRANIX	SYRINGE	SQ	Y
tbo-filgrastim	GRANIX	VIAL	SQ	Y
filgrastim-aafi	NIVESTYM	SYRINGE	SQ	N
filgrastim-aafi	NIVESTYM	VIAL	IJ	N
filgrastim-sndz	ZARXIO	SYRINGE	IJ	N
pegfilgrastim-apgf	NYVEPRIA	SYRINGE	SQ	N
pegfilgrastim-bmez	ZIEXTENZO	SYRINGE	SQ	N
pegfilgrastim-cbqv	UDENYCA	SYRINGE	SQ	N
pegfilgrastim-jmdb	FULPHILA	SYRINGE	SQ	N

Appendix 2: New Comparative Clinical Trials

A total of 61 citations were manually reviewed from the initial literature search. After further review, 60 citations were excluded because of wrong study design (eg, observational), comparator (eg, no control, placebo-controlled, or non-US medication), or outcome studied (eg, non-clinical). The remaining trial is summarized in the table below. Full abstract is included in **Appendix 3**.

Table 1. Description of Randomized Comparative Clinical Trials.

Study	Comparison	Population	Primary Outcome	Results
Waller et al.[21] Phase 3, MC, R, DB, PG, equivalence study Pharmacist preparing dose and clinician administering dose unblinded. Investigators and patients blinded.	1. MYL-1401H 6 mg (pegfilgrastim-jmdb, FULPHILA) 2. European Union-sourced reference pegfilgrastim 6 mg (NEULASTA) 2:1 randomization Received 24 hrs (+2 hr window) after end of chemo 6 planned chemo cycles every 3 weeks	Newly dx, ≥ 18 year old, Stage II/III breast Ca eligible to receive neoadjuvant/adjuvant TAC every 3 wks x 6 cycles N=194	CIN: Duration of severe neutropenia in cycle 1 (days with ANC < 0.5 x 10^9/L)	Mean (SD) 1. 1.2 days (0.93) 2. 1.2 days (1.0) MD -0.285 to 0.298 (within prespecified equivalence range with non-inferiority margin of 9%) Rates of TEAEs 1. 90% 2. 87% No deaths, treatment-related discontinuations, or suspected unexpected serious AE in either group.

Abbreviations: AE = adverse event; ANC = absolute neutrophil count; Ca = cancer; chemo = chemotherapy; CIN = chemotherapy induced neutropenia; DB = double-blind; Dx = diagnosed; hr = hour; MC = multicenter; MD = mean difference; PG = parallel-group; R= randomized; RCT = randomized clinical trial; SD = standard deviation; TAC = docetaxel/doxorubicin/cyclophosphamide; TEAE = treatment-emergent adverse events; wk = week.

Appendix 3: Abstracts of Comparative Clinical Trials

Waller, C. F., Ranganna, G. M., Pennella, E. J., Blakeley, C., Bronchud, M. H., Mattano, L. A., Jr., Berzoy, O., Voitko, N., Shparyk, Y., Lytvyn, I., Rusyn, A., Popov, V., Lang, I., Beckmann, K., Sharma, R., Baczkowski, M., Kothekar, M., Barve, A.

Randomized phase 3 efficacy and safety trial of proposed pegfilgrastim biosimilar MYL-1401H in the prophylactic treatment of chemotherapy-induced neutropenia

Pegfilgrastim is indicated for reducing the duration of neutropenia and incidence of febrile neutropenia in patients receiving cytotoxic chemotherapy. Here, safety and efficacy of MYL-1401H, a proposed pegfilgrastim biosimilar, were investigated as prophylaxis for chemotherapy-induced neutropenia. This was a phase 3, multicenter, randomized, double-blind, parallel-group equivalence trial of MYL-1401H vs European Union-sourced reference pegfilgrastim. Patients with newly diagnosed stage II/III breast cancer eligible to receive (neo) adjuvant chemotherapy with docetaxel/doxorubicin/cyclophosphamide every 3 weeks for 6 cycles were enrolled and randomized 2:1 to 6 mg of MYL-1401H or reference pegfilgrastim 24 h (+ 2-h window after the first 24 h) after the end of chemotherapy. The primary efficacy endpoint was the duration of severe neutropenia in cycle 1 (i.e., days with absolute neutrophil count (ANC) < 0.5 x 10⁹/L). Mean (standard deviation (SD)) duration of severe neutropenia in MYL-1401H and reference pegfilgrastim groups was 1.2 days (0.93) and 1.2 days (1.10), respectively. The 95% CI for least squares mean difference (- 0.285, 0.298) was within the predefined equivalence range of +/- 1 day. Secondary endpoints, including grade >= 3 neutropenia (frequency, 91% and 82% for MYL-1401H and reference pegfilgrastim, respectively), time to ANC nadir (mean (SD), 6.2 (0.98) and 6.3 (1.57) days), and duration of post-nadir recovery (mean (SD), 1.9 (0.85) and 1.7 (0.91) days) were comparable. Overall safety profiles of the study drugs were comparable. MYL-1401H demonstrated equivalent efficacy and similar safety to reference pegfilgrastim and may be an equivalent option for reducing incidence of neutropenia. (ClinicalTrials.gov , NCT02467868; EudraCT, 2014-002324-27).[21]

Appendix 4: Medline Search Strategy
Search performed 3/25/2021 Ovid

# ▲	Searches	Results
1	Filgrastim/ae, tu [Adverse Effects, Therapeutic Use]	259
2	pegfilgrastim.mp.	891
3	sargramostim.mp.	216
4	tbo-filgrastim.mp.	24
5	filgrastim-aafi.mp.	1
6	filgrastim-sndz.mp.	34
7	pegfilgrastim-apgf.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	1
8	pegfilgrastim-bmez.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	1
9	pegfilgrastim-cbqv.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	3
10	pegfilgrastim-jmdb.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	1
11	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10	1252
12	limit 11 to (adaptive clinical trial or clinical trial, all or clinical trial, phase iii or clinical trial, phase iv or comparative study or controlled clinical trial or guideline or meta analysis or multicenter study or practice guideline or pragmatic clinical trial or randomized controlled trial or "systematic review")	485
13	limit 12 to english language	477
14	limit 13 to yr="2018 -Current"	82

Appendix 5: Key Inclusion Criteria

Population	United States population
Intervention	G-CSF and GM-CSF in **Appendix 1**
Comparator	See **Appendix 1**
Outcomes	Symptom improvement, morbidity, mortality/survival, serious adverse events
Timing	Any study duration
Setting	Inpatient/outpatient combination or outpatient

Appendix 6: Summary of FDA labeled Indications of G-CSF and GM-CSF products

FDA Labeled Indications	Filgrastim NEUPOGEN[22]	Filgrastim-aafi NIVESTYM[23]	Filgrastim-sndz ZARXIO[19]	tbo-Filgrastim GRANIX[17]	Sargramostim LEUKINE*[24]
Decrease the **incidence** of infection, as manifested by febrile neutropenia, in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a significant incidence of severe neutropenia with fever.	x	x	x		
In adult and pediatric patients 1 month and older for reduction in the **duration** of severe neutropenia in patients with non-myeloid malignancies receiving myelosuppressive anticancer drugs associated with a clinically significant incidence of febrile neutropenia.				x	
Reduce the time to neutrophil recovery and the **duration** of fever, following induction or consolidation chemotherapy treatment of patients with acute myeloid leukemia (AML).	x	x	x		
To shorten time to neutrophil recovery and to reduce the **incidence** of severe and life-threatening infections and infections resulting in death following induction chemotherapy in adult patients 55 years and older with AML.					x
Reduce the **duration** of neutropenia and neutropenia-related clinical sequelae, e.g., febrile neutropenia, in patients with nonmyeloid malignancies undergoing myeloablative chemotherapy followed by bone marrow transplantation (BMT).	x	x	x		
For treatment of delayed neutrophil recovery or graft failure after autologous or allogeneic BMT in adult and pediatric patients 2 years of age and older.					x
For the acceleration of myeloid reconstitution following allogeneic BMT in adult and pediatric patients 2 years of age and older.					x

For the acceleration of myeloid reconstitution following autologous BMT or peripheral blood progenitor cell transplantation in adult and pediatric patients 2 years of age and older.					x
Mobilize autologous hematopoietic progenitor cells into the peripheral blood for collection by leukapheresis.	x	x	x		
For the mobilization of hematopoietic progenitor cells into peripheral blood for collection by leukapheresis and autologous transplantation in adult patients.					x
Reduce the incidence and duration of sequelae of severe neutropenia (e.g., fever, infections, oropharyngeal ulcers) in symptomatic patients with congenital neutropenia, cyclic neutropenia, or idiopathic neutropenia	x	x	x		
Increase survival in patients acutely exposed to myelosuppressive doses of radiation (Hematopoietic Syndrome of Acute Radiation Syndrome)	x				x
	Pegfilgrastim NEULASTA†[25]	**Pegfilgrastim-apgf NYVEPRIA†[2]**	**Pegfilgrastim-bmez ZIEXTENZO†[20]**	**Pegfilgrastim-cbqv UDENYCA†[26]**	**Pegfilgrastim-jmdb FULPHILA†[18]**
Decrease the incidence of infection, as manifested by febrile neutropenia, in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a clinically a significant incidence of febrile neutropenia.	x	x	x	x	X
Increase survival in patients acutely exposed to myelosuppressive doses of radiation (Hematopoietic Subsyndrome of Acute Radiation Syndrome).	x				

*Granulocyte Macrophage Colony Stimulating Factor (GM-CSF)

†Limitation of Use: NOT indicated for the mobilization of peripheral blood progenitor cells for hematopoietic stem cell transplantation.

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