Pharmacy Management Drug Policy

SUBJECT: Blood Modifiers
POLICY NUMBER: PHARMACY-79
EFFECTIVE DATE: 01/01/2019
LAST REVIEW DATE: 02/24/2024

If the member's subscriber contract excludes coverage for a specific service or prescription drug, it is not covered under that contract. In such cases, medical or drug policy criteria are not applied. This drug policy applies to the following line/s of business:

Policy Application

Category:	☒ Commercial Group (e.g., EPO, HMO, POS, PPO)	☒ Medicare Advantage
	☒ On Exchange Qualified Health Plans (QHP)	☐ Medicare Part D
	☒ Off Exchange Direct Pay	☒ Essential Plan (EP)
	☒ Medicaid & Health and Recovery Plans (MMC/HARP)	☒ Child Health Plus (CHP)
	☐ Federal Employee Program (FEP)	☐ Ancillary Services
	☒ Dual Eligible Special Needs Plan (D-SNP)	

DESCRIPTION:

Epoetin alfa is a protein that stimulates the production of red blood cells by the same mechanism as endogenous erythropoietin. It is administered as an intravenous or subcutaneous injection and has multiple FDA approved indications. Epoetin alfa is available as both an innovator biologic reference product and as a biosimilar.

Filgrastim and Pegfilgrastim are recombinant granulocyte colony-stimulating factors (G-CSF). CSF's act on hematopoietic cells and regulate the production of neutrophils within the bone marrow and affect neutrophil progenitor proliferation, differentiation, and selected end-cell functional activation. They are administered as an intravenous or subcutaneous injection and have multiple FDA approved indications. Both Filgrastim and Pegfilgrastim are available as innovator biologic reference products and as biosimilars.

For a biological product to be labeled as a biosimilar, it must be shown that it is highly similar and has no differences from an existing FDA approved reference product (i.e., Neulasta) by extensively analyzing the structure, purity, chemical identity, and bioactivity. It has been concluded that there are no clinically meaningful differences demonstrated through human pharmacokinetic/exposure and pharmacodynamic/responses, and assessment of immunogenicity. Biosimilars may be approved for all or a subset of the same indications as the reference product, depending on patent exclusivity. Biosimilars differ from generics in complexity, manufacturing processes, and in the data needed to demonstrate similarity for approval.

POLICY:

Based upon our criteria and review of the peer-reviewed literature treatment with the following medications is considered medically appropriate if administered in accordance with FDA guidelines

Epoetin alfa		
Drug	**FDA Approved Indications**	**Preferred Product**
Epogen Procrit Retacrit	• Treatment of anemia due to zidovudine in patients with HIV infection • Treatment of anemia due to chronic kidney disease (CKD) in patients on dialysis and not on dialysis • Treatment of anemia due to concomitant myelosuppressive chemotherapy. • Reduction of allogeneic red blood cell transfusions in patients undergoing elective, noncardiac, nonvascular surgery.	Retacrit and Procrit

A. Procrit and Retacrit are the preferred formulations of epoetin alfa and do not require prior authorization under the pharmacy or medical benefit.
B. Epogen does not require prior authorization under the medical or pharmacy benefit but may not be on all formularies.

Filgrastim		
Drug	**FDA Approved Indications**	**Preferred Product**
Granix	• 5B Myelosuppressive chemotherapy recipients with nonmyeloid malignancies	Zarxio
Neupogen	• 8B Acute myeloid leukemia following induction or consolidation chemotherapy • Bone marrow transplantation • Myelosuppressive chemotherapy recipients with nonmyeloid malignancies • Peripheral blood progenitor cell collection and therapy • 9BSevere chronic neutropenia	
Nivestym	• 11B Acute myeloid leukemia following induction or consolidation chemotherapy • Bone marrow transplantation • Myelosuppressive chemotherapy recipients with nonmyeloid malignancies • Peripheral blood progenitor cell collection and therapy • 12B Severe chronic neutropenia	
Releuko	• 14B Acute myeloid leukemia following induction or consolidation chemotherapy • Bone marrow transplantation • Myelosuppressive chemotherapy recipients with nonmyeloid malignancies • 15B Severe chronic neutropenia	
Zarxio	• 17B Acute myeloid leukemia following induction or consolidation chemotherapy • Bone marrow transplantation • Myelosuppressive chemotherapy recipients with nonmyeloid malignancies • Peripheral blood progenitor cell collection and therapy • Severe chronic neutropenia	

A. Zarxio is the preferred formulation of filgrastim and does not require prior authorization
B. Granix, Neupogen, Nivestym and Releuko all require prior authorization under both the medical benefit (administered by a heath care provider) and pharmacy benefit (self-administered), or may be non-formulary under the pharmacy benefit
C. All requests for FDA approved indications must be initiated and continued with Zarxio (Filgrastim-sndz) unless there is adequate medical justification as to why Zarxio cannot be used
    1. The use of Zarxio will not be required for the mobilization of donor hematopoietic progenitor cells in the allogeneic setting
    2. The use of Zarxio will not be required for pediatric patients who require a dose less than 180 mcg (0.3 mL)
D. All requests for Granix, Neupogen, Nivestym and Releuko for non-FDA approved indications will be evaluated based on off-label policy criteria. If clinical criteria are met, then Zarxio will be the required product

Pegfilgrastim		
Drug	**FDA Approved Indications**	**Preferred Products**
Fulphila	• Prevention of chemotherapy-induced neutropenia	Udenyca and Neulasta
Fylnetra	• Prevention of chemotherapy-induced neutropenia	
Neulasta	• Prevention of chemotherapy-induced neutropenia • Hematopoietic radiation injury syndrome	
Nyvepria	• Prevention of chemotherapy-induced neutropenia	
Rolvedon	• Prevention of chemotherapy-induced neutropenia	
Stimufend	• Prevention of chemotherapy-induced neutropenia	
Udenyca	• Prevention of chemotherapy-induced neutropenia • Hematopoietic radiation injury syndrome	
Ziextenzo	• Prevention of chemotherapy-induced neutropenia	

A. Medical Benefit

1. Neulasta and Udenyca are the preferred formulations of pegfilgrastim for Commercial, Exchange, Medicaid, Child Health Plus, Essential plan, and Medicare lines of business and do not require prior authorization.
2. Fulphila, Fylnetra, Nyvepria, Rolvedon, Stimufend, and Ziextenzo require prior authorization under the medical benefit (administered by a heath care provider) for Commercial, Exchange, Medicaid, Child Health Plus, Essential plan, and Medicare lines of business for New Starts **ONLY**

B. Pharmacy Benefit

1. Fulphila, Fylnetra, Nyvepria, Stimufend and Ziextenzo require prior authorization on the pharmacy benefit for Commercial, Exchange, and Child Health Plus formularies for New Starts **ONLY**
2. Rolvedon is not to be covered under the pharmacy benefit as it is only approved to be given by a healthcare professional

C. Coverage Criteria (for both Pharmacy and Medical benefit):

1. For a diagnosis of Febrile neutropenia prophylaxis following myelosuppressive chemotherapy the patient must meet the following requirements:
    a. The patient has a solid tumor or a non-myeloid malignancy, **AND**
    b. GCSF is administered 24-72 hours following myelosuppressive chemotherapy; **AND**
        i. The patient experienced a febrile neutropenic event with prior administration of the same or similar chemotherapy regimen, **OR**
        ii. The patient is receiving dose-dense myelosuppressive chemotherapy, **OR**
        iii. The patient is receiving myelosuppressive chemotherapy with a risk of febrile neutropenia of at least 20%, **OR**
        iv. The patient is receiving myelosuppressive chemotherapy with an intermediate risk of febrile neutropenia of 10-20%, **AND** one of the following risk factors:
            1. Persistent neutropenia (Absolute Neutrophil Count < 500/mm^3 or < 1000/mm^3 and expected to decline to less than 500/mm^3 within the next 48 hours)
            2. Bone marrow involvement by tumor
            3. Liver dysfunction with a total bilirubin > 2 mg/dL
            4. Renal dysfunction with a creatinine clearance < 50 mL/min
            5. Age > 65 years and receiving full chemotherapy dose intensity

6. History of extensive chemotherapy/radiation therapy **OR**

v. The patient is receiving myelosuppressive chemotherapy that has a low risk of febrile neutropenia of <10% **AND**
   1. Dose reduction is not clinically appropriate; **AND**
   2. At least two of the following risk factors are present:
      a. Persistent neutropenia (Absolute Neutrophil Count < 500/mm3 or < 1000/mm3 and expected to decline to less than 500/mm3 within the next 48 hours)
      b. Bone marrow involvement by tumor
      c. Liver dysfunction with a total bilirubin > 2 mg/dL
      d. Renal dysfunction with a creatinine clearance < 50 mL/min
      e. Age > 65 years and receiving full chemotherapy dose intensity
      f. History of extensive chemotherapy/radiation therapy **OR**

2. For a diagnosis of Wilms Tumor, the patient must meet the following requirements:
   a. Patient is scheduled to receive cyclophosphamide with etoposide, **OR**
   b. Patient is scheduled to receive combination therapy with cyclophosphamide, doxorubicin, and vincristine **OR**
3. For all other diagnoses, one of the following must be met:
   a. Approved by the U.S. Food and Drug Administration (FDA) **OR**
   b. A National Comprehensive Cancer Network (NCCN) category level 1 or 2A recommendation **OR**
   c. Satisfied by the criteria required for the applicable line of business (LOB) for the treatment of cancer in the Off-Label Use of FDA Approved Drugs policy (Pharmacy32) **AND**
4. All requests must be initiated and continued with Neulasta or Udenyca unless there is adequate medical justification as to why Neulasta and Udenyca cannot be used.

Cosela – trilaciclib (Medical)
1. Must be ≥ 18 years of age **AND** 2. Must be prescribed by an oncologist or hematologist **AND** 3. Must have a diagnosis of extensive-stage small cell lung cancer (EC-SCLC) **AND** 4. Must be administered on the same day as of one of the following chemotherapy regimens: a. Etoposide, carboplatin, and Tecentriq (atezolizumab) i. Cosela should be given on day 1, 2, and 3 of a 21-day cycle prior to etoposide administration for up to 4 cycles ii. Approval for this combination will be granted for 6 months 1. More than 4 cycles of this combination will not be granted as it has not been studied beyond 4 cycles of induction therapy b. Etoposide and carboplatin i. Cosela should be given on day 1, 2, and 3 of a 21-day cycle prior to etoposide administration until disease progression or unacceptable toxicities c. Topotecan i. Cosela should be given on days 1-5 of a 21-day cycle prior to topotecan administration until disease progression or unacceptable toxicities

POLICY GUIDELINES:

1. Approval time frames are as follows:

Line of Business	Medical Benefit Initial approval	Medical Recertification
SafetyNet (Medicaid, HARP, CHP, Essential Plan)	All sites of service – 6 months	All sites of service – 6 months
Commercial / Exchange	All sites of service – 6 months	All sites of service – 6 months
Medicare	All sites of service – 6 months	All sites of service – 6 months

Line of Business	Rx Benefit Initial approval	Rx recertification
Child Health Plus (CHP)	6 months * Does not apply to Medicaid and HARP	6 months * Does not apply to Medicaid and HARP
Commercial/Exchange	6 months * Does not apply to Medicaid and HARP	6 months * Does not apply to Medicaid and HARP

- Continued approval at time of recertification will require documentation that the drug is providing ongoing benefit to the patient in terms of improvement or stability in disease state or condition. Such documentation may include progress notes, imaging or laboratory findings, and other objective or subjective measures of benefit which support that continued use of the requested product is medically necessary. Also, ongoing use of the requested product must continue to reflect the current policy's preferred formulary. Recertification reviews may result in the requirement to try more cost-effective treatment alternatives as they become available (i.e., generics, biosimilars, or other guideline-supported treatment options). Requested dosing must continue to be consistent with FDA-approved or off-label/guideline-supported dosing recommendations.

2. Utilization Management are contract dependent and coverage criteria may be dependent on the contract renewal date. Additionally, coverage of drugs listed in this policy are contract dependent. Refer to specific contract/benefit language for exclusions.
3. For contracts where Insurance Law § 4903(c-1), and Public Health Law § 4903(3-a) are applicable, if trial of preferred drug(s) is the only criterion that is not met for a given condition, and one of the following circumstances can be substantiated by the requesting provider, then trial of the preferred drug(s) will not be required.
    - The required prescription drug(s) is (are) contraindicated or will likely cause an adverse reaction or physical or mental harm to the member;
    - The required prescription drug is expected to be ineffective based on the known clinical history and conditions and concurrent drug regimen;
    - The required prescription drug(s) was (were) previously tried while under the current or a previous health plan, or another prescription drug or drugs in the same pharmacologic class or with the same mechanism of action was (were) previously tried and such prescription drug(s) was (were) discontinued due to lack of efficacy or effectiveness, diminished effect, or an adverse event;
    - The required prescription drug(s) is (are) not in the patient's best interest because it will likely cause a significant barrier to adherence to or compliance with the plan of care, will likely worsen a comorbid condition, or will likely decrease the ability to achieve or maintain reasonable functional ability in performing daily activities;
    - The individual is stable on the requested prescription drug. The medical profile of the individual (age, disease state, comorbidities), along with the rational for deeming

stability as it relates to standard medical practice and evidence-based practice protocols for the disease state will be taken into consideration.
- The above criteria are not applicable to requests for brand name medications that have an AB rated generic. We can require a trial of an AB-rated generic equivalent prior to providing coverage for the equivalent brand name prescription drug.

4. This policy is applicable to drugs that are included on a specific drug formulary. If a drug referenced in this policy is non-formulary, please reference the Coverage Exception Evaluation Policy for All Lines of Business Formularies policy for review guidelines.
5. Dose and frequency should be in accordance with the FDA label or recognized compendia (for off-label uses). When the dose and/or frequency is requested in excess of established parameters, the request may be subject to an off-label review for medical necessity.

CODES:

Eligibility for reimbursement is based upon the benefits set forth in the member's subscriber contract. Codes may not be all inclusive as the AMA and CMS code updates may occur more frequently than policy updates.
Code Key: Experimental/Investigational = (E/I), Not medically necessary/ appropriate = (NMN).

Trade Name	Chemical Name	HCPCS Codes	Billing Unit
Epogen	Epoetin alfa	Q4081 – for ESRD (on dialysis) J0885 – for non-ESRD use	100 units 1000 units
Procrit	Epoetin alfa	Q4081 – for ESRD (on dialysis) J0885 – for non-ESRD use	100 units 1000 units
Retacrit	Epoetin alfa-epbx	Q5105 – for ESRD (on dialysis) Q5106 – for non-ESRD use	100 units 1000 units
Neupogen	Filgrastim	J1442	1 mcg
Granix	Tbo-filgrastim	J1446 J1447	5 mcg 1 mcg
Zarxio	Filgrastim-sndz	Q5101	1 mcg
Nivestym	Filgrastim-aafi	Q5110	1 mcg
Releuko	Filgrastim-ayow	Q5125	1 mcg
Neulasta	Pegfilgrastim	J2506	0.5 mg
Fulphila	Pegfilgrastim-jmdb	Q5108	0.5 mg
Udenyca	Pegfilgrastim-cbqv	Q5111	0.5 mg
Ziextenzo	Pegfilgrastim-bmez	Q5120	0.5 mg
Fylnetra	Pegfilgrastim-pbbk	Q5130	0.5 mg
Nyvepria	Pegfilgrastim-apgf	Q5122	0.5 mg
Stimufend	Pegfilgrastim-fpgk	Q5127	0.5 mg
Rolvedon	Eflapegrastim-xnst	J1449	0.1 mg
Cosela	Trilaciclib	C9078	1 mg

UPDATES:

Date	Revision
02/2024	Revised
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07/23	Revised
05/23	Revised

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10/22	Revised
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4/22	Revised
3/22	Revised
1/22	Revised
12/21	Revised
11/21	Revised
8/21	Revised
7/21	Revised and P&T Committee Approval
3/21	Revised
2/21	Revised
12/20	Revised
9/20	Revised and P&T Committee Approval
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5/20	Revised
12/19	Revised
7/19	Revised
5/19	Revised
12/18	P&T Committee Approval
11/18	Created

REFERENCES:

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3. Amgen Inc. Package Insert for Procrit. May 2012.
4. Pfizer Inc. Package Insert for Retacrit. May 2018.
5. Amgen Inc. Package Insert for Neupogen. June 2016.
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7. Sandoz Inc. Package Insert for Zarxio. February 2017.
8. Pfizer Labs Package Insert for Nivestym. July 2018.
9. Amgen Inc. Package Insert for Neulasta. June 2018
10. Mylan Package Insert for Fulphila. June 2018.
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12. Sandoz Inc. Package Insert for Ziextenzo. November 2019.
13. Pfizer Labs Package Insert for Nyvepria. June 2020.
14. G1 Therapeutics, Inc. Package Insert for Cosela. March 2021.