Pharmacy Management Drug Policy

SUBJECT: Blood Modifiers
POLICY NUMBER: PHARMACY-79
EFFECTIVE DATE: 01/01/2019
LAST REVIEW DATE: 12/02/2019

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. Medical or drug policies apply to commercial and Health Care Reform products only when a contract benefit for the specific service exists.

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.

Reblozyl (luspatercept-aamt), an erythroid maturation agent, is indicated for the treatment of anemia in adults with beta-thalassemia who require regular red blood cell (RBC) transfusions. Beta-thalassemia is an inherited blood disorder characterized by reduced levels of functional hemoglobin (Hb). Patients with a severe form (beta-thalassemia major) become symptomatic due to low Hb level (e.g., increased cardiac effort, tachycardia, poor growth) or ineffective erythropoiesis (e.g., bone changes, massive splenomegaly). Reblozyl (luspatercept-aamt) binds to select transforming growth factor-beta ligands to reduce aberrant Smad2/3 signaling and enhance late-stage erythropoiesis. By interfering with the signals that suppress RBC production, Reblozyl improves manufacture of RBCs and reduces the need for transfusions.

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.	Epogen, Procrit OR Retacrit

A. Epogen, Procrit and Retacrit are the preferred formulations of Epoetin alfa and do not require prior authorization

Filgrastim		
Drug	**FDA Approved Indications**	**Preferred Product**
Neupogen	• 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	Zarxio
Granix	• Myelosuppressive chemotherapy recipients with nonmyeloid malignancies	
Zarxio	• 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	
Nivestym	• 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 and Nivestym all require prior authorization both on the medical benefit (administered by a heath care provider) and pharmacy benefit (self-administered)
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.
    - Prior Authorization does not apply to Medicare members

D. Requested dose cannot exceed the following:
   - Myelosuppressive chemotherapy: 5mcg/kg/day
   - AML: 5mcg/kg/day
   - BMT: 10mcg/kg/day
   - Peripheral blood progenitor cell collection: 10 mcg/kg/day
   - Congenital Neutropenia: 12 mcg/kg/day (in rare instances, a higher dose may be needed)
   - Idiopathic or Cyclic Neutropenia 5mcg/kg/day

E. All requests for Granix, Neupogen and Nivestym 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
   - The use of Zarxio will not be required for the mobilization of donor hematopoietic progenitor cells in the allogeneic setting
   - The use of Zarxio will not be required for pediatric patients who require a dose less than 180 mcg (0.3 mL)

Pegfilgrastim		
Drug	**FDA Approved Indications**	**Preferred Product**
Fulphila	• Prevention of chemotherapy-induced neutropenia	Commercial/ Exchange: **Neulasta OR Udenyca** Medicaid/Child Health Plus: **Udenyca**
Neulasta	• Prevention of chemotherapy-induced neutropenia • Hematopoietic radiation injury syndrome	
Udenyca	• Prevention of chemotherapy-induced neutropenia	
Ziextenzo	• Prevention of chemotherapy-induced neutropenia	

A. Neulasta and Udenyca are the preferred formulations of Pegfilgrastim for **Commercial and Exchange** lines of business and do not require prior authorization
   - Fulphila and Ziextenzo require prior authorization on the medical benefit (administered by a heath care provider) for Commercial and Exchange lines of business for new starts on or after 01/01/2019
   - All requests for FDA approved indications must be initiated and continued with Neulasta or Udenyca unless there is adequate medical justification as to why Neulasta or Udenyca cannot be used.

B. Udenyca is the preferred formulation of Pegfilgrastim for **Medicaid and Child Health Plus** lines of business and does not require prior authorization
   - Fulphila, Neulasta, and Ziextenzo require prior authorization on the medical benefit (administered by a heath care provider) for Medicaid and Child Health Plus lines of business for new starts on or after 01/01/2019
   - All requests for FDA approved indications must be initiated and continued with Udenyca unless there is adequate medical justification as to why Udenyca cannot be used.

C. All requests for non-preferred products for non-FDA approved indications will be evaluated based on off-label policy criteria. If clinical criteria are met, then a preferred product (Udenyca or Neulasta, depending on line of business) will be the required product.

Anemia in Adults with Beta Thalassemia

Based upon our criteria and review of the peer-reviewed literature, treatment with **Reblozyl (luspatercept-aamt)** administered in accordance with FDA guidelines, has been medically proven to be an effective and well tolerated treatment for adult patients with beta thalassemia (also called Cooley's anemia) who require regular red blood cell (RBC) transfusions. Therefore, it is considered medically appropriate if all of the following criteria are met:

A. Patient must be at least 18 years of age
B. Patient must be followed by a hematologist or physician knowledgeable in the treatment of beta-thalassemia
C. Must have a diagnosis of beta thalassemia (including HbE/beta thalassemia and beta thalassemia combined with alpha-thalassemia)
    a. Reblozyl will not be covered for any other diagnoses including alpha thalassemia and sickle cell beta thalassemia (also known as hemoglobin S/β-thalassemia)
D. Patient must require regular RBC transfusions defined as:
    a. A need for at least 6 RBC units in the previous 24 weeks
    b. No transfusion-free period greater than 35 days in the previous 24 weeks
E. Reblozyl must be given by a healthcare professional and therefore, will only be covered under the medical benefit
F. Dosing should be initiated at 1 mg/kg every 3 weeks
    a. If there is no reduction in RBC transfusion burden after 6 weeks of treatment (2 doses) at 1 mg/kg dosing, the dose should be increased to 1.25 mg/kg every 3 weeks
    b. If there is no reduction in RBC transfusion burden after 9 weeks of treatment (3 doses) at the maximum dose (1.25 mg/kg every 3 weeks), treatment should be discontinued and will not be approved for additional administration
G. The maximum recommended dose is 1.25 mg/kg every 3 weeks. Requests for higher doses will not be approved.
H. Current body weight and requested dose regimen must be submitted for initial review and each recertification request
I. Initial approval will be granted for 6 months. Recertification will require documented reduction in RBC transfusion burden after receiving Reblozyl. Approval timeframes after the initial 6 months will be granted as outlined in the approval time frame table in the policy guideline section.

POLICY GUIDELINES:

1. Approval time frames are as follows:

Line of Business	**Medical Benefit Initial approval**	**Medical Recertification**
Medicaid Managed Care (MMC) / Child Health Plus (CHP)	6 months	12 months
Commercial / Exchange	Outpatient Hospital – 6 months	Outpatient Hospital – 6 months
	Home Care or Office Based – 2 years	Home Care or Office Based – 2 years

Line of Business	**Rx Benefit Initial approval**	**Rx recertification**
Medicaid Managed Care (MMC) / Child Health Plus (CHP)	2 years	2 years
Commercial/Exchange	2 years	2 years

- 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. Prior-authorization is contract dependent.

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.

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	1mcg
Granix	Tbo-filgrastim	J1446	5mcg
Zarxio	Filgrastim-sndz	Q5101	1mcg
Nivestym	Filgrastim-aafi	Q5110	1mcg
Neulasta	Pegfilgrastim	J2505	6mg
Fulphila	Pegfilgrastim-jmdb	Q5108	0.5mg
Udenyca	Pegfilgrastim-cbqv	Q5111	0.5mg
Reblozyl	Luspatercept-aamt		1 mg
Ziextenzo	Pegfilgrastim-bmez		

UPDATES:

Date	Revision
12/19	Revised
7/19	Revised
5/19	Revised
12/18	P&T Approval
11/18	Created

REFERENCES:

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12. Celgene Corporation Package Insert for Reblozyl. November 2019.
13. Sandoz Inc. Package Insert for Ziextenzo. November 2019.