This policy applies to the following:

	Standard Opt-in		PDPD		Marketplace		Medical Benefit	✓	Medicare Part B
	Standard Opt-out		ACSF		MMT		Medical Benefit: Biosimilars First		Medicare Part B: Biosimilars First
	VF		Balanced		Medical Benefit: Managed Medicaid		Medical Benefit: Add-on		Medicare Part B: Add-on

Reference #
3436-D

POLICY Document for EPOGEN, PROCRIT, RETACRIT

The overall objective of this policy is to support the appropriate and cost effective use of the medication, specific to use of preferred medication options, lower cost site of care and overall clinically appropriate use. This document provides specific information to each section of the overall policy.

Section 1: Preferred Product
- Policy information specific to preferred medications

Section 2: Clinical Criteria
- Policy information specific to the clinical appropriateness for the medication

Section 1: Preferred Product

EXCEPTIONS CRITERIA

ERYTHROPOIESIS STIMULATING AGENTS

PREFERRED PRODUCT: ARANESP AND RETACRIT

POLICY

This policy informs prescribers of preferred products and provides an exception process for targeted products through prior authorization.

I. PLAN DESIGN SUMMARY

This program applies to the erythropoiesis stimulating agents specified in this policy. Coverage for targeted products is provided based on clinical circumstances that would exclude the use of the preferred products and may be based on previous use of a product. The coverage review process will ascertain situations where a clinical exception can be made. This program applies to members who are new to treatment with a targeted product for the first time.

Each referral is reviewed based on all utilization management (UM) programs implemented for the client.

Table. Erythropoiesis stimulating agents

	Product(s)
Preferred	• **Aranesp** (darbepoetin alfa) • **Retacrit** (epoetin alfa)
Targeted	• **Epogen** (epoetin alfa) • **Mircera** (methoxy polyethylene glycol-epoetin beta) • **Procrit** (epoetin alfa)

II. EXCEPTION CRITERIA

This policy applies to the following:

	Standard Opt-in		**PDPD**		**Marketplace**		**Medical Benefit**	✓	**Medicare Part B**
	Standard Opt-out		**ACSF**		**MMT**		**Medical Benefit: Biosimilars First**		**Medicare Part B: Biosimilars First**
	VF		**Balanced**		**Medical Benefit: Managed Medicaid**		**Medical Benefit: Add-on**		**Medicare Part B: Add-on**

Reference #
3436-D

This program applies to members requesting treatment for an indication that is FDA-approved for the preferred products.

A. Mircera
Coverage for targeted product, Mircera, is provided when either of the following criteria is met:
1. Member has received treatment with the targeted product in the past 365 days.
2. Member has a documented inadequate response or intolerable adverse event with both of the preferred products, Aranesp and Retacrit.

B. Epogen or Procrit
Coverage for either of the targeted products, Epogen or Procrit, is provided when either of the following criteria is met:
1. Member has received treatment with the targeted product in the past 365 days.
2. Member meets both of the following criteria:
   a. Member has a documented inadequate response or intolerable adverse event with the preferred product, Aranesp, when prescribed for the treatment of anemia due to chronic kidney disease or the treatment of anemia due to myelosuppressive chemotherapy in cancer.
   b. Member has a documented intolerable adverse event with the preferred product, Retacrit, which was NOT an expected adverse event attributed to the active ingredient as described in the prescribing information.

Section 2: Clinical Criteria

STANDARD MEDICARE PART B MANAGEMENT

EPOGEN, PROCRIT, RETACRIT (epoetin alfa)

POLICY

I. INDICATIONS

This policy applies to the following:

	Standard Opt-in		**PDPD**		**Marketplace**		**Medical Benefit**	✓	**Medicare Part B**
	Standard Opt-out		**ACSF**		**MMT**		**Medical Benefit: Biosimilars First**		**Medicare Part B: Biosimilars First**
	VF		**Balanced**		**Medical Benefit: Managed Medicaid**		**Medical Benefit: Add-on**		**Medicare Part B: Add-on**

Reference #
3436-D

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
1. Epoetin alfa is indicated for the treatment of anemia due to chronic kidney disease (CKD), including patients on dialysis and not on dialysis to decrease the need for red blood cell (RBC) transfusion.
2. Epoetin alfa is indicated for the treatment of anemia due to zidovudine administered at ≤ 4200 mg/week in HIV-infected patients with endogenous serum erythropoietin levels of ≤ 500 mUnits/mL.
3. Epoetin alfa is indicated for the treatment of anemia in patients with non-myeloid malignancies where anemia is due to the effect of concomitant myelosuppressive chemotherapy, and upon initiation, there is a minimum of two additional months of planned chemotherapy.
4. Epoetin alfa is indicated to reduce the need for allogeneic RBC transfusions among patients with perioperative hemoglobin > 10 to ≤ 13 g/dL who are at high risk for perioperative blood loss from elective, noncardiac, nonvascular surgery. Epoetin alfa is not indicated for patients who are willing to donate autologous blood preoperatively.

Limitations of Use:
1. Epoetin alfa has not been shown to improve quality of life, fatigue, or patient well-being.
2. Epoetin alfa is not indicated for use:
   - In patients with cancer receiving hormonal agents, biologic products, or radiotherapy, unless also receiving concomitant myelosuppressive chemotherapy.
   - In patients with cancer receiving myelosuppressive chemotherapy when the anticipated outcome is cure.
   - In patients with cancer receiving myelosuppressive chemotherapy in whom the anemia can be managed by transfusion
   - In patients scheduled for surgery who are willing to donate autologous blood.
   - In patients undergoing cardiac or vascular surgery.
   - As a substitute for RBC transfusions in patients who require immediate correction of anemia.

Note: Use in members on dialysis is covered under the Medicare Part B dialysis benefit and is excluded from coverage under this policy.

B. Compendial Uses
1. Anemia in members with myelodysplastic syndromes
2. Anemia in congestive heart failure
3. Anemia in epidermolysis bullosa
4. Anemia in rheumatoid arthritis
5. Anemia due to hepatitis C treatment with ribavirin in combination with either interferon alfa or peginterferon alfa
6. Anemia in porphyria cutanea tarda
7. Anemia in members whose religious beliefs forbid blood transfusions
8. Beta thalassemia
9. Prophylaxis of anemia of prematurity
10. Treatment of iron overload

This policy applies to the following:

	Standard Opt-in		**PDPD**		**Marketplace**		**Medical Benefit**	✓	**Medicare Part B**
	Standard Opt-out		**ACSF**		**MMT**		**Medical Benefit: Biosimilars First**		**Medicare Part B: Biosimilars First**
	VF		**Balanced**		**Medical Benefit: Managed Medicaid**		**Medical Benefit: Add-on**		**Medicare Part B: Add-on**

Reference #
3436-D

11. Symptomatic anemia in members with primary myelofibrosis, post-polycythemia vera myelofibrosis, and post-essential thrombocythemia myelofibrosis
12. Anemia due to radiation
13. Anemia due to puerperium
14. Anemia due to multiple myeloma
15. Cancer patients who are undergoing palliative treatment

C. Nationally Covered Indication
Centers for Medicare and Medicaid Services guidelines provide coverage for epoetin alfa for anemia secondary to myelosuppressive chemotherapy based on the criteria in Sections II, III, and IV.

All other indications will be assessed on an individual basis. Submissions for indications other than those enumerated in this policy should be accompanied by supporting evidence from Medicare approved compendia.

II. EXCLUSIONS

The following exclusions criteria apply to members requesting use for anemia due to concomitant myelosuppressive chemotherapy:

A. The anemia is due to folate, B-12, or iron deficiency.
B. The anemia is due to hemolysis, bleeding, or bone marrow fibrosis.
C. The anemia is due to treatment for acute myelogenous leukemia, chronic myelogenous leukemia, or erythroid cancers.
D. The anemia is due to treatment with radiotherapy only.
E. Prophylactic use to prevent chemotherapy-induced anemia
F. Prophylactic use to reduce tumor hypoxia
G. Use in members with erythropoietin-type resistance due to neutralizing antibodies
H. Members with uncontrolled hypertension

III. CRITERIA FOR INITIAL APPROVAL

Note: Requirements regarding current hemoglobin level exclude values due to a recent transfusion.

A. Anemia due to chronic kidney disease
Authorization of 12 weeks may be granted for treatment anemia due to chronic kidney disease in members not receiving dialysis with a pretreatment hemoglobin of less than 10 g/dL or a hematocrit of less than 30%.

B. Anemia due to concomitant myelosuppressive chemotherapy
Authorization of 8 weeks may be granted for the treatment of anemia due to concomitant chemotherapy with all of the following criteria are met:

This policy applies to the following:

	Standard Opt-in		**PDPD**		**Marketplace**		**Medical Benefit**	✓	**Medicare Part B**
	Standard Opt-out		**ACSF**		**MMT**		**Medical Benefit: Biosimilars First**		**Medicare Part B: Biosimilars First**
	VF		**Balanced**		**Medical Benefit: Managed Medicaid**		**Medical Benefit: Add-on**		**Medicare Part B: Add-on**

Reference #
3436-D

1. The member is receiving chemotherapy for a solid tumor, multiple myeloma, lymphoma, or lymphocytic leukemia.
2. The hemoglobin level immediately prior to initiation or maintenance of therapy is less than 10 g/dL or the hematocrit is less than 30%.
3. The starting dose is not greater than 450 U/kg per week or 40,000 units weekly.

C. Reduction of allogeneic red blood cell transfusion in members undergoing elective, noncardiac, nonvascular surgery

Authorization of 12 weeks may be granted for members scheduled to have an elective, noncardiac, nonvascular surgery when the pretreatment hemoglobin is > 10 to ≤ 13 g/dL.

D. Anemia due to zidovudine in HIV-infected members

Authorization of 12 weeks may be granted for the treatment of anemia in members currently receiving zidovudine with pretreatment hemoglobin < 10 g/dL.

E. Anemia due to myelodysplastic syndrome

Authorization of 12 weeks may be granted for the treatment of anemia due to myelodysplastic syndrome with a pretreatment hemoglobin of less than 10 g/dL or a hematocrit of less than 30%.

F. Anemia in congestive heart failure

Authorization of 12 weeks may be granted for the treatment of anemia in members with congestive heart failure whose hemoglobin is less than 10 g/dL or whose hematocrit is less than 30%.

G. Anemia in epidermolysis bullosa

Authorization of 12 weeks may be granted for the treatment of anemia in members with epidermolysis bullosa whose hemoglobin is less than 10 g/dL or whose hematocrit is less than 30%.

H. Anemia in rheumatoid arthritis

Authorization of 12 weeks may be granted for the treatment of anemia in members with rheumatoid arthritis whose hemoglobin is less than 10 g/dL or whose hematocrit is less than 30%.

I. Anemia due to hepatitis C treatment

Authorization of 12 weeks may be granted for the treatment of anemia in members receiving treatment for hepatitis C who meet all of the following criteria:

1. The member's hemoglobin is less than 10 g/dL or hematocrit is less than 30%.
2. The member is receiving ribavirin in combination with either interferon alfa or peginterferon alfa.

J. Anemia in porphyria cutanea tarda

Authorization of 12 weeks may be granted for the treatment of anemia in members with porphyria cutanea tarda.

K. Anemia in members whose religious beliefs forbid blood transfusions

Authorization of 12 weeks may be granted for members whose religious beliefs forbid blood transfusions whose hemoglobin is less than 10 g/dL or whose hematocrit is less than 30%.

This policy applies to the following:

	Standard Opt-in		PDPD		Marketplace		Medical Benefit	✓	Medicare Part B
	Standard Opt-out		ACSF		MMT		Medical Benefit: Biosimilars First		Medicare Part B: Biosimilars First
	VF		Balanced		Medical Benefit: Managed Medicaid		Medical Benefit: Add-on		Medicare Part B: Add-on

Reference #
3436-D

L. Beta thalassemia
Authorization of 12 weeks may be granted for the treatment of anemia in members with beta thalassemia.

M. Prophylaxis of anemia of prematurity
Authorization of 12 weeks may be granted for the prophylaxis of anemia of prematurity in members less than 1 year of age.

N. Iron overload
Authorization of 12 weeks may be granted for the treatment of iron overload in combination with phlebotomy.

O. Anemia in myelofibrosis, post-polycythemia vera myelofibrosis, or post-essential thrombocythemia myelofibrosis
Authorization of 12 weeks may be granted for the treatment of anemia due to myelofibrosis, post-polycythemia vera myelofibrosis, or post-essential thrombocythemia myelofibrosis when all of the following criteria are met:
1. The member has a hemoglobin level of less than 10 g/dL or a hematocrit of less than 30%.
2. The member has an erythropoietin level of less than 500 mU/mL.

P. Anemia due to radiation
Authorization of 12 weeks may be granted for the treatment of anemia due to radiation.

Q. Anemia during the puerperium
Authorization of 12 weeks may be granted for the treatment of anemia following childbirth.

R. Anemia due to multiple myeloma
Authorization of 12 weeks may be granted for the treatment of anemia due to multiple myeloma.

1. Anemia due to cancer
Authorization of 12 weeks may be granted for members who have cancer and are undergoing palliative treatment.

IV. CONTINUATION OF THERAPY

Note: Requirements regarding current hemoglobin level exclude values due to a recent transfusion.

This policy applies to the following:

	Standard Opt-in		**PDPD**		**Marketplace**		**Medical Benefit**	✓	**Medicare Part B**
	Standard Opt-out		**ACSF**		**MMT**		**Medical Benefit: Biosimilars First**		**Medicare Part B: Biosimilars First**
	VF		**Balanced**		**Medical Benefit: Managed Medicaid**		**Medical Benefit: Add-on**		**Medicare Part B: Add-on**

Reference #
3436-D

All members (including new members) requesting authorization for continuation of therapy must be currently receiving therapy with the requested agent.

A. Authorization of 12 weeks may be granted for treatment of anemia due to concomitant myelosuppressive chemotherapy when all of the following criteria are met:
   1. The member is currently receiving therapy with epoetin alfa.
   2. The member does not have any exclusions listed in Section II.
   3. The member has experienced at least a 1 g/dL increase in their hemoglobin or a 3% increase in their hematocrit.
   4. Current hemoglobin is less than 11 g/dL or the prescriber will hold or reduce the dose of epoetin alfa to maintain a hemoglobin level sufficient to avoid transfusion.
   5. Treatment will not extend beyond 8 weeks following the final dose of myelosuppressive chemotherapy given in the member's current chemotherapy regimen.

B. Authorization of 12 weeks may be granted for all other indications when all of the following criteria are met:
   1. The member is currently receiving therapy with epoetin alfa.
   2. The member receiving epoetin alfa for an indication listed in Section III.
   3. Epoetin alfa has been effective for treating the diagnosis or condition.

V. REFERENCES

REFERENCES:

SECTION 1

1. Aranesp [package insert]. Thousand Oaks, CA: Amgen Inc.; January 2019.
2. Epogen [package insert]. Thousand Oaks, CA: Amgen Inc.; July 2018.
3. Procrit [package insert]. Horsham, PA: Janssen Products, LP; July 2018.
4. Mircera [package insert]. St. Gallen, Switzerland: Vifor (International) Inc.; June 2018.
5. Retacrit [package insert]. Lake Forest, IL: Hospira Inc.; January 2019.

SECTION 2

1. Epogen [package insert]. Thousand Oaks, CA: Amgen Inc.; July 2018.
2. Procrit [package insert]. Horsham, PA: Janssen Products.; July 2018.
3. Retacrit [package insert]. Lake Forest, IL: Hospira Inc.; January 2019.
4. National Comprehensive Cancer Network. The NCCN Drugs & Biologics Compendium. http://www.nccn.org. Accessed September 15, 2019.
5. Micromedex Solutions [database online]. Ann Arbor, MI: Truven Health Analytics Inc. Updated periodically. www.micromedexsolutions.com [available with subscription]. Accessed September 15, 2019.
6. Kidney Disease: Improving Global Outcomes (KDIGO) Anemia Work Group. KDIGO Clinical Practice Guideline for Anemia in Chronic Kidney Disease. Kidney Int. 2012; Suppl 2:279-335.

This policy applies to the following:

	Standard Opt-in		**PDPD**		**Marketplace**		**Medical Benefit**	✓	**Medicare Part B**
	Standard Opt-out		**ACSF**		**MMT**		**Medical Benefit: Biosimilars First**		**Medicare Part B: Biosimilars First**
	VF		**Balanced**		**Medical Benefit: Managed Medicaid**		**Medical Benefit: Add-on**		**Medicare Part B: Add-on**

Reference #
3436-D

7. National Kidney Foundation. KDOQI Clinical Practice Guideline and Clinical Practice Recommendations for Anemia in Chronic Kidney Disease: 2007 Update of Hemoglobin Target. http://www2.kidney.org/professionals/KDOQI/guidelines_anemiaUP/. Accessed September 15, 2019.
8. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Hematopoietic Growth Factors. Version 2.2019. http://www.nccn.org/professionals/physician_gls/pdf/growthfactors.pdf. Accessed September 13, 2019.
9. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Myelodysplastic Syndromes. Version 1.2020. http://www.nccn.org/professionals/physician_gls/pdf/mds.pdf. Accessed September 13, 2019.
10. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Myeloproliferative Neoplasms. Version 3.2019. http://www.nccn.org/professionals/physician_gls/pdf/mpn.pdf. Accessed September 13, 2019.
11. National Coverage Determination (NCD) for Erythropoiesis Stimulating Agents (ESAs) in Cancer and Related Neoplastic Conditions (110.21). Accessed September 29, 2019.