Medicare Part B Erythropoietins Prior Authorization

FDA APPROVED INDICATIONS AND DOSAGE[1-5]

Agent(s)	Indication(s)	Dosage
Aranesp® (darbepoetin alfa) Injection for intravenous or subcutaneous use	• Anemia due to chronic kidney disease (CKD), including patients on dialysis and patients not on dialysis	**Anemia due to CKD:** **Adult:** Dialysis patient dosing is 0.45 mcg/kg body weight IV or SC once weekly or 0.75 mcg/kg IV or SC every 2 weeks. In adult patients not receiving dialysis, the recommended starting dose is 0.45 mcg/kg body weight IV or SC may be administered at 4 week intervals **Pediatric:** Dialysis patient dosing is 0.45 mcg/kg body weight SC or IV once weekly. Pediatric patients not on dialysis may be initiated at a dose of 0.75 mcg/kg once every 2 weeks
	• 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 Limitations of Use: Aranesp has not been shown to improve quality of life, fatigue, or patient well-being Aranesp 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	**Anemia due to chemotherapy:** 2.25 mcg/kg SC weekly **or** 500 mcg SC every 3 weeks May be increased to 4.5 mcg/kg SC weekly

Agent(s)	Indication(s)	Dosage
	in whom the anemia can be managed by transfusion ● As a substitute for red blood cell transfusions in patients who require immediate correction of anemia	
Epogen® (epoetin alfa) Injection for intravenous or subcutaneous	● Anemia due to Chronic Kidney Disease (CKD), in patients on dialysis and those not on dialysis to decrease the need for red blood cell (RBC) transfusion	**Anemia due to CKD:** **Adult:** 50-100 Units/kg SC or IV 3 times weekly. Individualize maintenance dose **Pediatric:** starting 50 Units/kg SC or IV 3 times weekly (children on dialysis). Individualize maintenance dose
	● Treatment of anemia due to zidovudine administered at ≤ 4200 mg/week in HIV-infected patients with endogenous serum erythropoietin levels of ≤ 500 mUnits/mL	**Zidovudine treated patients with HIV:** **Initial dosing:** 100 Units/kg SC or IV 3 times weekly. May increase dose to a maximum of 300 Units/kg 3 times weekly
	● 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 2 additional months of planned chemotherapy	**Anemia in patients with non-myeloid malignancies:** **Three times weekly dosing** Initial dose: 150 Units/kg SC 3 times weekly. May increase dose to a maximum of 300 Units/kg SC 3 times weekly **Weekly Dosing** **Adults:** 40,000 Units SC Max: 60,000 Units SC. **Pediatrics (≥5 years old):** 600 Units/kg IV (maximum 40,000 Units) Max: 900 Units/kg IV weekly (maximum 60,000 Units)
	● Reduce the need of 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 Limitations of Use: Epogen has not been shown to improve quality of life, fatigue, or patient well-being Epogen is not indicated for use	**Surgery Patients:** 300 Units/kg/day SC for 10 days before surgery, on the day of surgery, and for 4 days after surgery (15 days total). **OR** 600 Units/kg SC once weekly doses (21, 14, and 7 days before surgery) plus a fourth dose on the day of surgery

Agent(s)	Indication(s)	Dosage
	• 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	
Mircera® (methoxy polyethylene glycol – epoetin beta) Injection for intravenous or subcutaneous use	• Anemia associated with chronic kidney disease (CKD) in adult patients on dialysis and not on dialysis • Anemia associated with chronic kidney disease in pediatric patients 5 to 17 years of age on hemodialysis who are converting from another erythropoiesis stimulating agent (ESA) after their hemoglobin level was stabilized with an ESA Limitations of Use: Mircera has not been shown to improve quality of life, fatigue, or patient well-being Mircera is not indicated and is not recommended for use:	**Adult patients:** **Initial:** 0.6 mcg/kg body weight SC or IV once every two weeks **Conversion from another ESA:** dosed once monthly or once every two weeks based on total weekly epoetin alfa or darbepoetin alfa dose at time of conversion **Pediatric patients with CKD on hemodialysis:** **Switching from epoetin alfa:** 4 times previous weekly epoetin alfa dose (units)/125 **Switching from darbepoetin alfa:** 4 times previous weekly darbepoetin alfa dose (mcg)/0.55

Agent(s)	Indication(s)	Dosage
	• In the treatment of anemia due to cancer chemotherapy • As a substitute for RBC transfusions in patients who require immediate correction of anemia	
Procrit® (epoetin alfa) Injection for intravenous or subcutaneous use	• Anemia due to chronic kidney disease (CKD), in patients on dialysis and those not on dialysis to decrease the need for red blood cell (RBC) transfusion	**Anemia due to CKD:** **Adult:** 50-100 Units/kg SC or IV 3 times weekly. Individualize maintenance dose **Pediatric:** starting 50 Units/kg SC or IV 3 times weekly (children on dialysis). Individualize maintenance dose
	• Treatment of anemia due to zidovudine administered at ≤ 4200 mg/week in HIV-infected patients with endogenous serum erythropoietin levels of ≤ 500 mUnits/mL	**Zidovudine treated patients with HIV:** **Initial dosing:** 100 Units/kg SC or IV 3 times weekly. May increase dose to a maximum of 300 Units/kg 3 times weekly
	• 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 2 additional months of planned chemotherapy	**Anemia in patients with non-myeloid malignancies:** **Three times weekly dosing** Initial dose: 150 Units/kg SC 3 times weekly. May increase dose to a maximum of 300 Units/kg SC 3 times weekly **Weekly Dosing** **Adults:** 40,000 Units SC Max: 60,000 Units SC **Pediatrics (≥5 years old):** 600 Units/kg IV (maximum 40,000 Units) Max: 900 Units/kg IV weekly (maximum 60,000 Units)
	• Reduce the need of 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 Limitations of Use: Procrit has not been shown to improve quality of life, fatigue, or patient well-being Procrit is not indicated for use:	**Surgery Patients:** 300 Units/kg/day SC for 10 days before surgery, on the day of surgery, and for 4 days after surgery (15 days total) OR 600 Units/kg SC once weekly doses (21, 14, and 7 days before surgery) plus a fourth dose on the day of surgery

Agent(s)	Indication(s)	Dosage
	• 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	
Retacrit® (epoetin alfa-epbx) Injection for intravenous or subcutaneous use	• Anemia due to Chronic Kidney Disease (CKD), in patients on dialysis and those not on dialysis to decrease the need for red blood cell (RBC) transfusion	**Anemia due to CKD:** **Adult:** 50-100 Units/kg SC or IV 3 times weekly. Individualize maintenance dose **Pediatric:** starting 50 Units/kg SC or IV 3 times weekly (children on dialysis). Individualize maintenance dose
	• Treatment of anemia due to zidovudine administered at ≤ 4200 mg/week in HIV-infected patients with endogenous serum erythropoietin levels of ≤ 500 mUnits/mL	**Zidovudine treated patients with HIV:** **Initial dosing:** 100 Units/kg SC or IV 3 times weekly. May increase dose to a maximum of 300 Units/kg SC or IV 3 times weekly
	• 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 2 additional months of planned chemotherapy	**Anemia in patients with non-myeloid malignancies:** **Three times weekly dosing** Initial dose: 150 Units/kg SC 3 times weekly. May increase dose to a maximum of 300 Units/kg SC 3 times weekly **Weekly Dosing** **Adults:** 40,000 Units SC Max: 60,000 Units SC. **Pediatrics (≥5 years old):** 600 Units/kg IV (maximum 40,000 Units)

Agent(s)	Indication(s)	Dosage
		Max: 900 Units/kg IV weekly (maximum 60,000 Units)
	• Reduce the need of 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 Limitations of Use: Retacrit has not been shown to improve quality of life, fatigue, or patient well-being Retacrit 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	**Surgery Patients:** 300 Units/kg/day SC for 10 days before surgery, on the day of surgery, and for 4 days after surgery (15 days total). **OR** 600 Units/kg SC once weekly doses (21, 14, and 7 days before surgery) plus a fourth dose on the day of surgery **Evaluation of Iron Stores and Nutritional Factors:** Evaluate the iron status in all patients before and during treatment. Administer supplemental iron therapy when serum ferritin is less than 100 mcg/L or when serum transferring saturation is less than 20%

IV – intravenous; SC-subcutaneous

CLINICAL RATIONALE

The pathophysiologic origins of anemia can be grouped into three categories 1) decreased production of functional red blood cells (RBCs); 2) increased destruction of RBCs; and 3) blood loss. Anemia is characterized by a decrease in hemoglobin (Hb) concentration, RBC count, and/or hematocrit (Hct) to subnormal levels. Treatment of anemia depends on disease severity and etiology. Treatment options include vitamins and/or mineral supplementation, treatment with erythropoietin therapy, and blood transfusion.[10]

The National Cancer Institute categorizes anemia into 4 active grades:[10]

Grade	**Scale** (hemoglobin level in g/dL)
1 (mild)	10 - < lower limit of normal
2 (moderate)	8 - <10
3 (severe)	6.5 - <8
4 (life threatening)	<6.5

Erythropoietin has the same biological effects as endogenous erythropoietin therefore, stimulates RBC production in the bone marrow.[2,4]

Darbepoetin differs from epoetin alfa only in two additional N-glycosylation sites which results in an increased half-life.[1] When given in equipotent dosing, efficacy between epoetin and darbepoetin is considered similar. A report by the Agency for Healthcare Research and Quality (AHRQ) comparing effectiveness of the two agents when used to manage anemia in patients undergoing cancer treatment concluded there were no clinically significant differences in hemoglobin response, transfusion reduction, or thromboembolic events.[6] The American Society of Clinical Oncology/American Society of Hematology (ASCO/ASH) clinical practice guideline updated in 2010 considers epoetin and darbepoetin to be equivalent with respect to both efficacy and safety.[7] The National Comprehensive Cancer Network (NCCN) guidelines for Cancer- and Chemotherapy - induced anemia note that either darbepoetin or epoetin alfa can be used in ESA therapy.[10]

NCCN notes that a biosimilar is a biological product that is highly similar to the FDA-approved originator product with the exception of minor differences in clinically inactive components and no differences regarding efficacy, safety, and purity. Biosimilars have the same amino acid sequence; however, they may differ at the protein level due to the nature and complexity of biologic products. If overall safety and efficacy remain unaffected, biosimilars may be approved for the same indications and can be substituted for the originator product.[10]

Although the equipotent doses have not been conclusively determined, the prescribing information for darbepoetin provides the following conversion chart from epoetin alfa to darbepoetin.[1]

Previous Weekly Epoetin alfa Dose (Units/week)	**Weekly darbepoetin dose (mcg/week)**	
	Adult	**Pediatric**
<1500	6.25	The available data are insufficient to determine a darbepoetin dose
1500 to 2499	6.25	6.25
2500 to 4999	12.5	10
5000 to 10999	25	20
11000 to 17999	40	40
18000 to 33999	60	60
34000 to 89999	100	100
≥ 90000	200	200

The Mircera prescribing information provides the following conversion chart from epoetin alfa or darbepoetin alfa to Mircera in patients with CKD.[3]

		Mircera Dose

Previous Weekly Epoetin alfa Dose (units/week)	Previous Weekly Darbepoetin alfa Dose (mcg/week)	Once Monthly (mcg/month)	Once Every Two Weeks (mcg/every two weeks)
<8000	<40	120	60
8000-16000	40-80	200	100
>16000	>80	360	180

Anemia associated with Chronic Kidney Disease (CKD)
Anemia in patients with CKD occurs due the kidneys inability to produce sufficient amounts of erythropoietins. KDIGO (Kidney Disease Improving Global Outcomes) Clinical Practice guidelines recommend the following as it pertains to use of ESAs:[13]

- For CKD patients NOT on dialysis (ND) and a Hb of ≥10.0 g/dl, the agency does not recommend ESA therapy be initiated
- For CKD ND patients with Hb < 10.0 g/dl, the decision to use ESA should be patient specific and based on a risk/benefit ratio
- For CKD patients in stage 5D, ESA use is recommended to prevent Hb falling below 9.0 g/dl. The agency recommends starting therapy when the hemoglobin is between 9.0 and 10.0 g/dl
- In general, ESAs should not be used to maintain Hb >11.5 g/dl in adults with CKD.
- For pediatric patients, the recommendation to use ESA therapy should be patient specific and based on a risk/benefit ratio
- For all pediatric CKD patients on ESA therapy, Hb concentration should be maintained in the range of 11.0-12.0 g/dl

The current United States guidelines (KDOQI) note that the selection of hemoglobin target and selection of the hemoglobin level at which ESA therapy is initiated in the individual patient should include consideration of potential benefits (including improvement in quality of life and avoidance of transfusion) and potential harms (including the risk of life threatening adverse events); in dialysis and non-dialysis patients with chronic kidney disease (CKD) receiving ESA therapy. These guidelines state that in dialysis and non-dialysis patients with CKD receiving ESA therapy, the selected Hb target should generally be in the range of 11.0 to 12.0 g/dL.[8,9,12]

Chemotherapy Induced Anemia[10]
Causes of anemia in patients with cancer are often multifactorial. Anemia may be attributed to underlying comorbidities such as bleeding, hemolysis, nutritional deficiencies, hereditary disease, renal insufficiency, hormone dysfunction, or a combination of these factors. The malignancy itself can also lead to or exacerbate anemia in several ways.

There is a wide variation in Hb levels among healthy subjects and a universal "normal level is difficult to define. According to the NCCN panel, an Hb level ≤ 11 g/dL should prompt an evaluation of anemia in a patient with cancer. For patient with a high baseline level, a drop ≥ 2 g/dL is also cause for concern and assessment. Any other cause of anemia that may be rectified independent of cancer therapy should be treated as indication. When no such etiology is identified, the effects of cancer-related inflammation and/or myelosuppressive chemotherapy (if applicable) should be considered the cause of anemia.

The decision regarding the best treatment option is dependent on many factors. While packed red blood cell transfusion is best for symptomatic patients requiring an immediate boost in Hb levels, consideration of ESA therapy and/or iron supplementation may be warranted for the long-term management of anemia in high-risk patients or in asymptomatic patients with comorbidities.

Special categories in considering ESA use from The National Comprehensive Cancer Network (NCCN) are:

- Patients with cancer and CKD (moderate to severe): Consider treatment with ESAs by FDA dosing/dosing adjustments
- Patient undergoing palliative treatment: consider treatment with ESAs by FDA dosing/dosing adjustments, RBC transfusion, or clinical trial based on patient preferences
- Patients with cancer not receiving therapy, receiving non-myelosuppressive chemotherapy, or myelosuppressive chemotherapy with curative intent (e.g. early-stage breast cancer, Hodgkin lymphoma, non-Hodgkin's lymphoma, testicular cancer, early-stage non-small cell lung cancer, small cell lung cancer): ESAs not recommended
- The ESA dose should be adjusted for each patient to maintain the lowest hemoglobin level sufficient to avoid red blood transfusion and/or to bring about gradual improvement in anemia related symptoms
- Studies have reported decreased survival in patients with cancer receiving ESA for anemia where target Hb levels are greater than 12 g/dL
- Patients with ferritin values > 800 mg/mL or a transferrin saturation (TSAT) ≥ 50% are not iron deficient and these patients do not require iron supplementation or ESA therapy

Myelodysplastic Syndrome

NCCN Clinical Practice Guideline for Myelodysplastic Syndromes states:[14]

- ESA have been used safely in large numbers of adult MDS patients and have become important for symptomatic improvement of those affected by the anemia caused by this disease often with a decrease in RBC transfusion requirements. Studies assessing the long-term use of epoetin with or without G-CSF in MDS compared to historical or randomized controls haven't shown a negative impact on survival or AML evaluation. Studies have shown improved survival in low-risk MDS patients with low transfusion need treated with these agents
- An alternative option to lenalidomide may include an initial trial of ESAs in patients with serum Epo levels of 500 mU/ml or less. Patients with normal cytogenetics and with <15% marrow ringed sideroblasts and serum Epo levels 500 mu/mL or less may respond to Epo if relatively high doses are used (40,000-60,000 units 1-3 times a week)

In general, the ASCO/ASH guidelines recommend starting and modifying doses of ESA follow FDA guidelines. However, the guidelines note that for the use of epoetin and darbepoetin in adult cancer patients, consideration must be given to demonstrate risks of thromboembolism, the possibility of death, and minimizing ESA use, particularly in patients with malignancy being treated with curative intent. Also, although the FDA label now limits the indication for ESA use to patients receiving chemotherapy for palliative intent, no study has evaluated outcomes of ESA therapy by subgroups defined by chemotherapy intent. Determination of the goal of treatment requires clinical judgement in many cases. Use of epoetin or darbepoetin is recommended at hemoglobin concentrations that have decreased to less than 10 g/dL to decrease transfusions.[11]

If hemoglobin is $\geq$10 g/dL but <12 g/dL, treatment should be determined by clinical judgment, consideration of the risks and benefits of ESAs, and patient's preferences. Hemoglobin can be increased to the lowest concentration needed to avoid transfusions. Continuing epoetin or darbepoetin beyond 6-8 weeks in the absence of response does not seem to be beneficial.[7,11]

Surgery

Epoetin alfa is indicated for the treatment of anemic patients (hemoglobin >10 to $\leq$13 g/dL) who are at high risk for perioperative blood loss from elective, noncardiac, nonvascular surgery to reduce the need for allogeneic blood transfusions.[2,3]

Anemia in HIV
The causes of HIV-related anemia are multifactorial. HIV may directly affect bone marrow stromal cell or cause cytokine secretion, leading to decreased production of red blood cells (RBCs) and other bone marrow elements. Many drugs used to treat HIV-related disorders are myelosuppressive but severe anemia is most often related to the use of zidovudine. Patients most likely to respond to ESA treatment have a serum erythropoietin level <500 iu/L.[15,16]

Safety
The prescribing information for the ESAs notes that in controlled trials, patients experienced a greater risk of death, serious adverse cardiovascular reactions, and stroke when given ESAs to a target hemoglobin level of greater than 11 g/dL. Additionally, no trial has identified a hemoglobin target level, ESA dose, or dosing strategy that does not increase these risks.[1-5]

- Aranesp (darbepoetin alfa) is contraindicated in:
  - Uncontrolled hypertension
  - Pure red cell aplasia (PRCA) that begins after treatment with any ESA
  - Serious allergic reactions to Aranesp
- Epogen (epoetin alfa) is contraindicated in:
  - Uncontrolled hypertension
  - Pure red cell aplasia (PRCA) that begins after treatment with any ESA
  - Serious allergic reactions to Epogen
  - Use of multi-dose vial in neonates, infants, pregnant women, and nursing mothers (contains benzyl alcohol)
- Mircera (methoxy polyethylene glycol – epoetin beta) is contraindicated in:
  - Uncontrolled hypertension
  - Pure red cell aplasia (PRCA) that begins after treatment with Mircera or other erythropoietin protein drugs
  - History of serious or severe allergic reactions to Mircera (e.g. anaphylactic reactions, angioedema, bronchospasm, skin rash, and urticaria)
- Procrit (epoetin alfa) is contraindicated in:
  - Uncontrolled hypertension
  - Pure red cell aplasia (PRCA) that begins after treatment with any ESA
  - Serious allergic reactions to Procrit
  - Use of multi-dose vial in neonates, infants, pregnant women, and nursing mothers (contains benzyl alcohol)
- Retacrit (epoetin alfa-epbx) is contraindicated in:
  - Uncontrolled hypertension
  - Pure red cell aplasia (PRCA) that begins after treatment with Retacrit or other erythropoietin protein drugs
  - Serious allergic reactions to Retacrit or other epoetin alfa products
  - Use of multiple-dose vials containing benzyl alcohol in neonates, infants, pregnant women, and lactating women

References

1. Aranesp prescribing information. Amgen Inc. January 2019.
2. Epogen prescribing information. Amgen Inc. July 2018.
3. Mircera prescribing information. Genentech, Inc. June 2018.
4. Procrit prescribing information. Amgen Inc. July 2018.
5. Retacrit prescribing information. Pfizer Biosimilars. September 2020.
6. Grant MD, Piper M, Bohlius J, et al. Epoetin and Darbepoetin for Managing Anemia in Patients Undergoing Cancer Treatment: Comparative Effectiveness Update. Rockville (MD): Agency for Healthcare Research and Quality (US); 2013 Apr. Report No: 13-EHC077-EF.

7. Rizzo JD, Somerfield MR, Hagerty KL, et al. Use of epoetin and darbepoetin in patients with cancer: 2007 American Society of Clinical Oncology/American Society of Hematology clinical practice guideline update. *J Clin Oncol.* 2008;26(1):132-149.
8. KDOQI. National Kidney Foundation. Clinical practice recommendations for anemia in chronic kidney disease in children. *Am J Kidney Dis*. 2006;47(5 Suppl 3): s86-108.
9. KDOQI. National Kidney Foundation. Clinical practice recommendations for anemia in chronic kidney disease in adults. *Am J Kidney Dis*. 2006;47(5 Suppl 3): s16-85.
10. NCCN Clinical Practice Guidelines in Oncology. Hematopoietic Growth Factors. Version 2.2020
11. Rizzo JD, Brouwers M, Hurley P, et al. American Society of Hematology/American Society of Clinical Oncology clinical practice guideline update on the use of epoetin and darbepoetin in adult patients with cancer. *Blood* 2010; 116: 4045-4059.
12. KDOQI Clinical Practice Guideline and Clinical Practice Recommendations for Anemia in Chronic Kidney Disease: 2012 Update of Hemoglobin Target.
13. KDIGO Clinical Practice Guidelines for Anemia in Chronic Kidney Disease. Kidney Int Suppl 2012 Aug;2(4):279-335.
14. NCCN Clinical Practice Guidelines in Oncology. Myelodysplastic syndromes. Version 3.2021.
15. Claster S. Biology of Anemia, differential diagnosis, and Treatment Options in Human Immunodeficiency Virus Infection. The Journal of Infectious diseases, Volume 185, Issue Supplement_2, 15 May 2002, Pages S105-S109.
16. Volberding PA, Levine AM, Dieterich D, et al. Anemia in HIV Infection: Clinical Impact and Evidence-Based Management Strategies. Clinical Infectious Diseases. 2004;38:1454-63.

Document History
Original Prime Standard Part B criteria, approved by P&TUM Committee 06/2021
Mid-Year Review Prime Standard Part B criteria, with changes to criteria approved by P&T UM Committee 12/2021

Medicare Part B Erythropoietins

TARGET PREFERRED AGENT(S)	TARGET NON-PREFERRED AGENT(S)
Target preferred and non-preferred agent(s) to be determined client	Target preferred and non-preferred agent(s) to be determined client
Aranesp (darbepoetin alfa) **Epogen** (epoetin alfa) **Mircera** (methoxy polyethylene glycol – epoetin beta) **Procrit** (epoetin alfa) **Retacrit** (epoetin alfa-epbx)	

Brand (generic)	GPI	Multisource Code	HCPCS Code
Aranesp (darbepoetin alfa)			
10 mcg/0.4 mL	8240101510E510	M, N, O, or Y	J0881, J0882
25 mcg/mL	82401015102010	M, N, O, or Y	J0881, J0882
25 mcg/0.42 mL	8240101510E528	M, N, O, or Y	J0881, J0882
40 mcg/mL	82401015102020	M, N, O, or Y	J0881, J0882
40 mcg/0.4 mL	8240101510E543	M, N, O, or Y	J0881, J0882
60 mcg/mL	82401015102030	M, N, O, or Y	J0881, J0882
60 mcg/0.3 mL	8240101510E552	M, N, O, or Y	J0881, J0882
100 mcg/mL	82401015102040	M, N, O, or Y	J0881, J0882
100 mcg/0.5 mL	8240101510E560	M, N, O, or Y	J0881, J0882
150 mcg/0.3 mL	8240101510E575	M, N, O, or Y	J0881, J0882
200 mcg/mL	82401015102060	M, N, O, or Y	J0881, J0882
200 mcg/0.4 mL	8240101510E582	M, N, O, or Y	J0881, J0882
300 mcg/mL	82401015102070	M, N, O, or Y	J0881, J0882
300 mcg/0.6 mL	8240101510E588	M, N, O, or Y	J0881, J0882
500 mcg/mL	8240101510E590	M, N, O, or Y	J0881, J0882
Epogen, **Procrit (epoetin alfa)**			
2000 U/mL	82401020002010	M, N, O, or Y	J0885, Q4081
3000 U/mL	82401020002015	M, N, O, or Y	J0885, Q4081
4000 U/mL	82401020002020	M, N, O, or Y	J0885, Q4081
10,000 U/mL	82401020002040	M, N, O, or Y	J0085, Q4081
20,000 U/mL	82401020002050	M, N, O, or Y	J0885, Q4081
40,000 U/mL	82401020002060	M, N, O, or Y	J0885, Q4081
Mircera (methoxy polyethylene glycol – epoetin beta)			
30 mcg/0.3mL	8240104010E510	M, N, O, or Y	J0887, J0888
50 mcg/0.3mL	8240104010E515	M, N, O, or Y	J0887, J0888
75 mcg/0.3mL	8240104010E520	M, N, O, or Y	J0887, J0888
100 mcg/0.3mL	8240104010E525	M, N, O, or Y	J0887, J0888
150 mcg/0.3mL	8240104010E535	M, N, O, or Y	J0887, J0888
200 mcg/0.3mL	8240104010E545	M, N, O, or Y	J0887, J0888
Retacrit (epoetin alfa-epbx)			
2,000 U/mL	82401020042010	M, N, O, or Y	Q5105, Q5106
3,000 U/mL	82401020042015	M, N, O, or Y	Q5105, Q5106
4,000 U/mL	82401020042020	M, N, O, or Y	Q5105, Q5106
10,000 U/mL	82401020042040	M, N, O, or Y	Q5105, Q5106
20,000 U/mL	82401020042050	M, N, O, or Y	Q5105, Q5106
40,000 U/mL	82401020042060	M, N, O, or Y	Q5105, Q5106

CRITERIA FOR APPROVAL

Evaluation

Target Agent(s) will be approved when ALL of the following are met:

1. The requested agent is being used for ONE of the following:
    a. An FDA approved indication
    OR
    b. An indication in CMS approved compendia

    AND
2. If the client has preferred agents, then ONE of the following:
    a. The requested agent is the preferred agent
    OR
    b. Information has been provided that indicates the patient has been treated with the requested agent in the past 365 days
    OR
    c. There is documentation that the patient has had an ineffective treatment response to the active ingredient(s) of ALL preferred agent(s)
    OR
    d. The patient has a documented intolerance, hypersensitivity, or FDA labeled contraindication to the active ingredient(s) of ALL preferred agent(s)
    OR
    e. The prescriber has submitted documentation indicating ALL preferred agent(s) are likely to be ineffective or are likely to cause an adverse reaction or other harm to the patient

    AND
3. The patient does NOT have any FDA labeled contraindications to the requested agent
    AND
4. The requested quantity (dose) is within FDA labeled dosing or supported in compendia for the requested indication

Length of Approval: up to 12 months