Harvard Pilgrim Health Care – Pharmacy Prior Authorization Guideline

Guideline Name	**Hematinic Agents**: Aranesp (darbepoetin alfa), Epogen (epoetin alfa), Procrit (epoetin alfa), Retacrit (epoetin alfa-epbx), Mircera (methoxy peg-epoetin beta)

1. Criteria

Product Name: Aranesp	
Approval Length	12 Week(s)
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 - ONE of the following:

1.1 - ALL of the following:

1.1.1 - Prescribed for the treatment of anemia due to ONE of the following conditions:
- Chronic kidney disease (CKD)
- Patient whose religious beliefs forbid blood transfusions
- Cancer and receiving palliative treatment

AND

1.1.2 - Patient has a documented pre-treatment hemoglobin level less than 10g/dL*

OR

1.2 - ALL of the following:

1.2.1 - Prescribed for the treatment of anemia due to Primary Myelofibrosis (MF), Post-polycythemia Vera MF, Post-Essential Thrombocythemia MF, or Myelodysplastic Syndrome (MDS)

AND

1.2.2 - Pre-treatment serum erythropoietin level less than 500mU/mL

AND

1.2.3 - Patient has a documented pre-treatment hemoglobin level less than 10g/dL*

OR

1.3 - ALL of the following:

1.3.1 - Prescribed for the treatment of anemia due to myelosuppressive chemotherapy for a non-myeloid malignancy without a curative intent

AND

1.3.2 - There are at least two additional months of planned chemotherapy

AND

1.3.3 - Hemoglobin level immediately prior to ESA initiation or within the last four weeks of maintenance ESA treatment is less than 10g/dL or hematocrit is less than 30%

AND

1.3.4 - Iron stores must be replete with a transferrin saturation (TSAT) greater than or equal to 20% or a ferritin greater than or equal to 100 ng/mL within the last 4 months

OR

1.4 - ALL of the following:

1.4.1 - Prescribed for the treatment of anemia associated with Myelodysplastic Syndrome (MDS)

AND

1.4.2 - Pre-treatment serum erythropoietin level is less than 500 mU/mL

AND

1.4.3 - Pre-treatment hemoglobin level is less than 10gm/dL* or hematocrit is less than 30%

Notes	*Requirements regarding pretreatment hemoglobin level exclude values due to a recent transfusion

Product Name: Aranesp	
Approval Length	12 Week(s)^
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 - ONE of the following:

1.1 - Patient has not yet completed 12-weeks of treatment

OR

1.2 - ALL of the following:

1.2.1 - Anemia due to ONE of the following conditions:

- Chronic kidney disease (CKD)
- Patient whose religious beliefs forbid blood transfusions
- Primary Myelofibrosis (MF), Post-polycythemia Vera MF, or Post-Essential Thrombocythemia MF
- Cancer and receiving palliative treatment

AND

1.2.2 - Current hemoglobin is less than or equal to 12g/dL

AND

1.2.3 - Response to therapy is noted with a hemoglobin increase of at least 1g/dL from baseline

OR

1.3 - ALL of the following:

1.3.1 - Prescribed for the treatment of anemia due to myelosuppressive chemotherapy for a non-myeloid malignancy

AND

1.3.2 - There are at least two additional months of planned chemotherapy

AND

1.3.3 - Hemoglobin level immediately prior to ESA initiation or within the last four weeks of maintenance ESA treatment is less than 10g/dL or hematocrit is less than 30%

AND

1.3.4 - Iron stores must be replete with a transferrin saturation (TSAT) level greater than or equal to 20% or a ferritin level greater than or equal to 100 ng/mL within the last 4 months

AND

1.3.5 - There was an increase in hemoglobin greater than or equal to 1 g/dL or an increase in hematocrit greater than or equal to 3% compared to pretreatment baseline after 8 weeks of treatment

OR

1.4 - ALL of the following:

1.4.1 - Prescribed for the treatment of anemia associated with Myelodysplastic Syndrome (MDS)

AND

1.4.2 - Serum erythropoietin level is less than or equal to 500 mU/mL

AND

1.4.3 - Hemoglobin is less than or equal to 12g/dL or hematocrit is less than or equal to 36% within the last 4 weeks of maintenance ESA therapy

AND

1.4.4 - Iron stores must be replete with a transferrin saturation (TSAT) level greater than or equal to 20% or a ferritin level greater than or equal to 100 ng/mL within the last 4 months

AND

1.4.5 - There was an increase in hemoglobin greater than or equal to 1 g/dL or an increase in hematocrit greater than or equal to 3% after 8 weeks of treatment

Notes	^12 weeks or up to 12 weeks for patients who did not complete the initial 12 weeks of therapy.

Product Name: Epogen, Procrit, or Retacrit	
Approval Length	12 Week(s)^
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization

Approval Criteria

1 - BOTH of the following:

1.1 - Prescribed for the treatment of anemia due to ONE of the following conditions:

- Chronic kidney disease (CKD)
- Rheumatoid arthritis (RA)
- Hepatitis C treatment and the patient is receiving ribavirin in combination with either interferon alfa or peginterferon alfa
- Zidovudine in HIV-infected patients with a pre-treatment serum erythropoietin level < 500 mU/mL
- Patient whose religious beliefs forbid blood transfusions
- Primary Myelofibrosis (MF), Post-polycythemia Vera MF, or Post-Essential Thrombocythemia MF with symptomatic anemia and a pre-treatment serum erythropoietin level < 500mU/mL
- Cancer and receiving palliative therapy

AND

1.2 Patient has a pre-treatment hemoglobin less than 10gm/dL*

OR

2 - Prescribed for the treatment of anemia due to Congestive Heart Failure (CHF) with a pre-treatment hemoglobin level less than 9g/dL*

OR

3 - Prescribed for the treatment of reduction of allogeneic red blood cell transfusion in a patient undergoing elective, non-cardiac, nonvascular surgery with a pre-treatment hemoglobin less than 13g/dL*

OR

4 - ALL of the following:

4.1 - Prescribed for the treatment of anemia due to myelosuppressive chemotherapy for a non-myeloid malignancy without a curative intent

AND

4.2 - There are at least two additional months of planned chemotherapy

AND

4.3 - Hemoglobin level immediately prior to ESA initiation or within the last four weeks of maintenance ESA treatment is less than 10g/dL and/or hematocrit is less than 30%

AND

4.4 - Iron stores must be replete with a transferrin saturation (TSAT) greater than or equal to 20% or a ferritin level greater than or equal to 100 ng/mL within the last 4 months

OR

5 - ALL of the following:

5.1 - Prescribed for the treatment of anemia associated with Myelodysplastic Syndrome (MDS)

AND

5.2 - Pre-treatment serum erythropoietin level is less than 500 mU/mL

AND

5.3 - Pre-treatment hemoglobin level is less than 10gm/dL* or hematocrit less than 30%

Notes	*Requirements regarding pretreatment hemoglobin level exclude values due to a recent transfusion. ^12 weeks or 30 days for treatment of reduction of allogeneic red blood cell transfusion in a patient undergoing elective, non-cardiac, nonvascular surgery

Product Name: Epogen, Procrit, or Retacrit	
Approval Length	12 Week(s)^
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization

Approval Criteria

1 - ONE of the following:

1.1 Patient has not yet completed 12-weeks of treatment

OR

1.2 ALL of the following:

1.2.1 Anemia due to ONE of the following conditions:

- Chronic kidney disease (CKD)
- Congestive Heart Failure (CHF)
- Rheumatoid arthritis (RA)
- Hepatitis C patient receiving ribavirin in combination with either interferon alfa or peginterferon alfa
- HIV-infected patient receiving Zidovudine
- Religious beliefs forbid blood transfusions
- Primary Myelofibrosis (MF), Post-polycythemia Vera MF, or Post-Essential Thrombocythemia MF
- Cancer and receiving palliative treatment

AND

1.2.2 Current hemoglobin is less than or equal to 12g/dL

AND

1.2.3 Response to therapy is noted with a hemoglobin increase of at least 1g/dL from baseline

OR

2 - ALL of the following:

2.1 - Prescribed for the treatment of anemia due to myelosuppressive chemotherapy for a non-myeloid malignancy

AND

2.2 - There are at least two additional months of planned chemotherapy

AND

2.3 - Hemoglobin level immediately prior to ESA initiation or within the last four weeks of maintenance ESA treatment is less than 10g/dL or hematocrit is less than 30%

AND

2.4 - Iron stores must be replete with a transferrin saturation (TSAT) greater than or equal to 20% or a ferritin level greater than or equal to 100 ng/mL within the last 4 months

AND

2.5 - There was an increase in hemoglobin greater than or equal to 1 g/dL or an increase in hematocrit greater than or equal to 3% compared to pretreatment baseline after 8 weeks of treatment

OR

3 - ALL of the following:

3.1 - Prescribed for the treatment of anemia associated with Myelodysplastic Syndrome (MDS)

AND

3.2 - Serum erythropoietin level is less than or equal to 500 mU/mL

AND

3.3 - Hemoglobin is less than or equal to 12g/dL or hematocrit is less than or equal to 36% within the last 4 weeks of maintenance ESA therapy

AND

3.4 - Iron stores must be replete with a transferrin saturation (TSAT) level greater than or equal to 20% or a ferritin level greater than or equal to 100 ng/mL within the last 4 months

AND

3.5 - There was an increase in hemoglobin greater than or equal to 1 g/dL or an increase in hematocrit greater than or equal to 3% after 8 weeks of treatment

Notes	^12 weeks or up to 12 weeks for patients who did not complete the initial 12 weeks of therapy

Product Name: Mircera	
Approval Length	12 Week(s)
Therapy Stage	Initial Authorization
Guideline Type	Prior Authorization, Non-Formulary

Approval Criteria

1 - Prescribed for the treatment of anemia due to chronic kidney disease in a patient with a pre-treatment hemoglobin level less than 10g/dL*

Notes	*Requirements regarding pretreatment hemoglobin level exclude values due to a recent transfusion

Product Name: Mircera	
Approval Length	12 Week(s)^
Therapy Stage	Reauthorization
Guideline Type	Prior Authorization, Non-Formulary

Approval Criteria

1 - ONE of the following:

1.1 Patient has not yet completed 12 weeks of treatment

OR

1.2 ALL of the following:

1.2.1 Response to therapy is noted with a rise in hemoglobin of at least 1gm/dL from baseline (excludes values due to recent transfusion)

AND

1.2.2 Treatment of anemia due to chronic kidney disease

AND

1.2.3 Current hemoglobin is less than or equal to 12gm/dL

Notes	^12 weeks or up to 12 weeks for patients who did not complete the initial 12 weeks of therapy

2. Background

Benefit/Coverage/Program Information

RATIONALE
To ensure the appropriate use of these agents as indicated and demonstrated by low hemoglobin levels. Safety of these products has been questioned when the hemoglobin is above 11g/dL.

FDA Approved Indications
Epoetin alfa (Epogen, Procrit) 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.
- Anemia due to zidovudine administered at ≤ 4200 mg/week in HIV-infected patients with endogenous serum erythropoietin levels of ≤ 500 mUnits/mL.
- 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.

Epoetin alfa is indicated to reduce the need for allogeneic red blood cell (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 willing to donate autologous blood preoperatively.

Limitations of Use:
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 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.

Aranesp (darbepoetin) is indicated for:

- Treatment of anemia due to chronic kidney disease (CKD), including patients on dialysis and patients not on dialysis.
- 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.

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.

- As a substitute for RBC transfusions in patients who require immediate correction of anemia

Mircera (methoxy polyethylene glycol-epoetin beta) is indicated for the treatment of anemia associated with chronic kidney disease (CKD) in:

- adult patients on dialysis and adult patients not on dialysis
- pediatric patients 5 to 17 years of age on hemodialysis who are converting from another ESA after their hemoglobin level was stabilized with an ESA.

Limitations of Use:
Mircera is not indicated and is not recommended for use:

- In the treatment of anemia due to cancer chemotherapy
- As a substitute for RBC transfusions in patients who require immediate correction of anemia

REFERENCES

- Aranesp [package insert]. Thousand Oaks, CA: Amgen Inc. January 2019.
- Epogen [package insert]. Thousand Oaks, CA: Amgen Inc. July 2018.
- Mircera [package insert]. Vifor (International) Inc. St. Gallen, Switzerland. June 2018.
- Procrit [package insert]. Horsham, PA: Janssen Products. July 2018.
- Retacrit [package insert]. Lake Forest, IL: Hospira Inc; June 2020.
- National Comprehensive Cancer Network. The NCCN Drugs & Biologics Compendium. http://www.nccn.org. Accessed September 19, 2018.
- Micromedex Solutions [database online]. Ann Arbor, MI: Truven Health Analytics Inc. Updated periodically. www.micromedexsolutions.com [available with subscription]. Accessed September 19, 2018.
- AHFS DI (Adult and Pediatric) [database online]. Hudson, OH: Lexi-Comp, Inc.; http://online.lexi.com/lco/action/index/dataset/complete_ashp [available with subscription]. Accessed September 19, 2018.
- 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.
- 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 19, 2018.
- National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Cancer- and Chemotherapy-Induced Anemia. Version 3.2018. http://www.nccn.org/professionals/physician_gls/pdf/anemia.pdf. Accessed September 19, 2018.
- Rizzo JD, Brouwers M, Hurley P, et al. American Society of Clinical Oncology/American Society of Hematology clinical practice guideline update on the use of epoetin and darbepoetin in adult patients with cancer. *J Clin Oncol.* 2010;28(33):4996-5010.
- National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Myelodysplastic Syndromes. Version 1.2019. http://www.nccn.org/professionals/physician_gls/pdf/mds.pdf. Accessed September 18, 2018.

- Qaseem A, Humphrey LL, Fitterman N, Starkey M, Shekelle P, for the Clinical Guidelines Committee of the American College of Physicians. Treatment of Anemia in Patients with Heart Disease: A Clinical Practice Guideline from the American College of Physicians. *Ann Intern Med*. 2013;159:770-779.
- National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Myeloproliferative Neoplasms. Version 1.2019. https://www.nccn.org/professionals/physician_gls/pdf/mpn.pdf. Accessed September 18, 2018.
- Cervantes F, Alvarez-Larran A, Hernandez-Boluda JC, et al. Erythropoietin treatment of the anemia of myelofibrosis with myeloid metaplasia: results in 20 patients and review of the literature. Br J Haematol. 2004;127(4):399-403.

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