HARVARD PILGRIM HEALTH CARE
RECOMMENDED MEDICATION REQUEST GUIDELINES

HEMATINIC AGENTS

Generic	Brand	HICL	GCN	Exception/Other
DARBEPOETIN ALFA IN POLYSORBATE	ARANESP	22890		
EPOETIN ALFA	EPOGEN, PROCRIT	04553		
EPOETIN ALFA-EPBX	RETACRIT	44931		
METHOXY PEG-EPOETIN BETA	MIRCERA	35005		

GUIDELINES FOR USE

NOTE: Requirements regarding pretreatment hemoglobin level exclude values due to a recent transfusion.

ARANESP

1. Is the request for initial treatment?

   If yes, continue to #2.
   If no, continue to #4.

2. Is the request for the treatment of anemia due to **ONE** of the following conditions?
   - Chronic kidney disease (CKD)
   - Myelosuppressive chemotherapy **AND** meets each of the following:
     - The patient has nonmyeloid malignancy
     - The intent of chemotherapy is non-curative
   - Myelodysplastic Syndrome (MDS)
   - Patient's whose religious beliefs forbid blood transfusions
   - Primary Myelofibrosis (MF), Post-polycythemia Vera MF, or Post-Essential Thrombocythemia MF **AND** meets each of the following:
     - The patient has symptomatic anemia
     - Pre-treatment serum erythropoietin level < 500mU/mL

   If yes, continue to #3.
   If no, do not approve. Please use status code #238 and the denial text provided:
   DENIAL TEXT: Per your health plan's Hematinic Agents guideline, Aranesp is only covered when prescribed for the treatment of anemia due to one of the following conditions:
   - Chronic kidney disease (CKD)
   - Myelosuppressive chemotherapy **AND** you met the following:
     - You have nonmyeloid malignancy
     - The intent of chemotherapy is non-curative
   - Myelodysplastic Syndrome (MDS)
   - Your religious beliefs forbid blood transfusions
   - Primary Myelofibrosis (MF), Post-polycythemia Vera MF, or Post-Essential Thrombocythemia MF **AND** you met the following:
     - You have symptomatic anemia
     - Pre-treatment serum erythropoietin level < 500mU/mL

   Your provider did not indicate that **[you are being treated for one of these conditions or select criteria not met]** and therefore your request was not approved.

CONTINUED ON NEXT PAGE

HEMATINIC AGENTS

GUIDELINES FOR USE - ARANESP (CONTINUED)

3. Does the patient have a documented pre-treatment hemoglobin level less than 10g/dL?

   If yes, continue to #7.
   If no, do not approve. Please use status code #238 and the denial text provided.
   DENIAL TEXT: Per your health plan's Hematinic Agents guideline, confirmation of a hemoglobin level less than 10g/dL is required prior to approving coverage of Aranesp for your condition and therefore your request was not approved.

4. Is the request for a patient who has not yet completed 12-weeks of treatment?

   If yes, continue to #7.
   If no, continue to #5.

5. Is the request for a patient who meets **ALL** of the following?
   - Anemia due to **ONE** of the following conditions:
     - Chronic kidney disease (CKD)
     - Myelodysplastic Syndrome (MDS)
     - Patient's whose religious beliefs forbid blood transfusions
     - Primary Myelofibrosis (MF), Post-polycythemia Vera MF, or Post-Essential Thrombocythemia MF
   - Current hemoglobin is less than or equal to 12g/dL
   - Response to therapy is noted with a hemoglobin increase of at least 1g/dL

   If yes, continue to #7.
   If no, continue to #6.

CONTINUED ON NEXT PAGE

GUIDELINES FOR USE - ARANESP (CONTINUED)

6. Is the request for a patient who is being treated for anemia due to Myelosuppressive chemotherapy **AND** meets **ALL** of the following?
   - The patient has nonmyeloid malignancy
   - The intent of chemotherapy is non-curative
   - Current hemoglobin is less than 11g/dL
   - Response to therapy is noted with a hemoglobin increase of at least 1g/dL from baseline

   If yes, continue to #7.
   If no, do not approve. Please use status code #238 and the denial text provided:
   DENIAL TEXT: Per your health plan's Hematinic Agents guideline, authorization for renewal requires documentation of each of the following:
   - Current hemoglobin level less than or equal to 12gm/dL **OR** less than equal to 11gm/dL if your anemia is due to Myelosuppressive chemotherapy
   - Response to therapy with a rise in your hemoglobin level of at least 1gm/dL after receiving 12 weeks of therapy
   - Prescribed for the treatment of anemia due to one of the following conditions:
     - Chronic kidney disease (CKD)
     - Myelodysplastic Syndrome (MDS)
     - Your religious beliefs forbid blood transfusions
     - Primary Myelofibrosis (MF), Post-polycythemia Vera MF, or Post-Essential Thrombocythemia MF
     - Myelosuppressive chemotherapy with nonmyeloid malignancy **AND** the intent of chemotherapy is non-curative

   Your provider did not submit documentation that **[meet these conditions or select specific criteria not met]** and therefore your request was not approved.

7. **Approve by HICL for 12 weeks. (The quantity is hard-coded for 4 syringes/vials per fill.)**
   Please use status code #056 and the approval text provided.
   APPROVAL TEXT: Aranesp (darbepoetin) has been approved for a quantity of 4 [syringes/vials] per prescription fill for a 12-week period.

EPOGEN, PROCRIT or RETACRIT

1. Is the request for initial treatment?

   If yes, continue to #2.
   If no, continue to #6.

CONTINUED ON NEXT PAGE

HEMATINIC AGENTS

GUIDELINES FOR USE - EPOGEN, PROCRIT or RETACRIT (CONTINUED)

2. Is the request for the treatment of anemia due to **ONE** of the following conditions?
   - Chronic kidney disease (CKD)
   - Myelosuppressive chemotherapy with nonmyeloid malignancy and the intent of chemotherapy is non-curative
   - Myelodysplastic Syndrome (MDS)
   - 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
   - Patient's 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

   If yes, continue to #5.
   If no, continue to #3.

3. Is the request for the treatment of anemia due to Congestive Heart Failure (CHF) with a pre-treatment hemoglobin level less than 9g/dL?

   If yes, continue to #9.
   If no, continue to #4.

4. Is the request 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 level greater than 10g/dL and less than 13g/dL?

   If yes, continue to #9.
   If no, do not approve. Please use status code #238 and the denial text provided.
   DENIAL TEXT: Per your health plan's Hematinic Agents guideline, **[requested medication]** is only covered when prescribed for the treatment of anemia due to one of the following conditions:
   - Chronic kidney disease (CKD)
   - Myelosuppressive chemotherapy with nonmyeloid malignancy and the intent of chemotherapy is non-curative
   - Myelodysplastic Syndrome (MDS)
   - 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
   - Patients whose religious beliefs forbid blood transfusions

   (Denial text continued on next page)

CONTINUED ON NEXT PAGE

GUIDELINES FOR USE - EPOGEN, PROCRIT, or RETACRIT (CONTINUED)

- Primary Myelofibrosis (MF), Post-polycythemia Vera MF, or Post-Essential Thrombocythemia MF with symptomatic anemia and a pre-treatment serum erythropoietin level < 500mU/mL
- Congestive Heart Failure (CHF) with a pre-treatment hemoglobin level less than 9g/dL
- Reduction of allogeneic red blood cell transfusion in a patient undergoing elective, noncardiac, nonvascular surgery with a pre-treatment hemoglobin level greater than 10g/dL and less than 13g/dL

Your provider did not indicate that **[you are being treated for one of these conditions or select criteria not met]** and therefore your request was not approved.

5. Does the patient have a pre-treatment hemoglobin less than 10gm/dL?

If yes, continue to #9.
If no, do not approve. Please use status code #238 and the denial text provided.
DENIAL TEXT: Per your health plan's Hematinic Agents guideline, confirmation of a pre-treatment hemoglobin less than 10gm/dL is required, prior to approving coverage of **[requested drug]** and is only covered when prescribed for the treatment of anemia for specific conditions, such as:

- Chronic kidney disease (CKD)
- Myelosuppressive chemotherapy with nonmyeloid malignancy and the intent of chemotherapy is non-curative
- Myelodysplastic Syndrome (MDS)
- Rheumatoid arthritis (RA)
- Hepatitis C treatment and you are receiving ribavirin in combination with either interferon alfa or peginterferon alfa
- You are a HIV-infected patient receiving Zidovudine
- Your 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

Your provider did not indicate that **[you are being treated for one of these conditions or select criteria not met]** and therefore your request was not approved.

CONTINUED ON NEXT PAGE

HEMATINIC AGENTS

GUIDELINES FOR USE – EPOGEN, PROCRIT, or RETACRIT (CONTINUED)

6. Is the request for a patient who has not yet completed 12 weeks of treatment?

   If yes, continue to #9.
   If no, continue to #7.

7. Is the request for a patient who meets all of the following?
   - Anemia due to **ONE** of the following:
     - Chronic kidney disease (CKD)
     - Myelodysplastic Syndrome (MDS)
     - 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
   - Current hemoglobin is less than or equal to 12g/dL
   - Response to therapy is noted with a hemoglobin increase of at least 1g/dL from baseline

   If yes, continue to #9.
   If no, continue to #8.

8. Is the request for a patient who is being treated for anemia due to Myelosuppressive chemotherapy **AND** meets all of the following?
   - The patient has a nonmyeloid malignancy
   - The intent of chemotherapy is non-curative
   - The current hemoglobin is < 11g/dL
   - Response to therapy is noted with a hemoglobin increase of at least 1g/dL from baseline

   If yes, continue to #9.
   If no, do not approve. Please use status code #238 and the denial text provided:
   DENIAL TEXT: Per your health plan's Hematinic Agents guideline, **[requested medication]** authorization for renewal requires documentation of each of the following:
   - Current hemoglobin level less than or equal to 12gm/dL **OR** less than or equal to 11gm/dL if your anemia is due to Myelosuppressive chemotherapy
   - Response to therapy with a rise in your hemoglobin level of at least 1gm/dL from baseline after receiving 12 weeks of therapy

   (Denial text continued on next page)

CONTINUED ON NEXT PAGE

HEMATINIC AGENTS

GUIDELINES FOR USE - EPOGEN, PROCRIT, or RETACRIT (CONTINUED)

- When prescribed for the treatment of anemia due to one of the following conditions:
  - Chronic kidney disease (CKD)
  - Myelodysplastic Syndrome (MDS)
  - Congestive Heart Failure (CHF)
  - Rheumatoid arthritis (RA)
  - Hepatitis C patient receiving ribavirin in combination with either interferon alfa or peginterferon alfa
  - HIV-infected and receiving Zidovudine
  - Your religious beliefs forbid blood transfusions
  - Primary Myelofibrosis (MF), Post-polycythemia Vera MF, or Post-Essential Thrombocythemia MF
  - Myelosuppressive chemotherapy with nonmyeloid malignancy **AND** the intent of chemotherapy is non-curative

  Your provider did not indicate that you are being treated for a covered condition and therefore your request was not approved.

9. **Approve by HICL for 12 weeks.** Please use status code #056 and the approval text provided.
   APPROVAL TEXT: [Requested medication] has been approved for a quantity of [# vials] per prescription fill for a 12-week period.
   The quantity is hard-coded for EPOGEN, PROCRIT, AND RETACRIT for 12 vials per fill with the exception of the following:
   - **EPOGEN 20,000/ML VIAL: (The quantity is hard-coded for 4 vials per fill.)**
   - **PROCRIT 20,000/ML VIAL and 40,000/ML VIAL: (The quantity is hard-coded for 4 vials per fill.)**
   - **RETACRIT 40,000/ML VIAL: (The quantity is hard-coded for 4 vials per fill.)**

MIRCERA

1. Is the request for initial treatment?

   If yes, continue to #2.
   If no, continue to #3.

CONTINUED ON NEXT PAGE

HEMATINIC AGENTS

GUIDELINE FOR USE - MIRCERA (CONTINUED)

2. Is the request for the treatment of anemia due to chronic kidney disease in a patient with a pre-treatment hemoglobin level < 10g/dL?

   If yes, **approve by HICL for 12 weeks.** Please use status code #057 and the approval text provided.
   APPROVAL TEXT: Mircera has been approved for your condition for a 12-week period.

   If no, do not approve. Please use status code #238 and the denial text provided:
   DENIAL TEXT: Per your health plan's Hematinic Agents guideline, Mircera is only covered when prescribed for the treatment of anemia due to chronic kidney disease in a patient with a pre-treatment hemoglobin level less than 10gm/dL. Your provider did not submit documentation that you **[meet these conditions or select the specific criteria not met]** and therefore your request was not approved.

3. Is the request for a patient who has not yet completed 12 weeks of treatment?

   If yes, **approve by HICL for 12 weeks.** Please use status code #057 and the approval text provided.
   APPROVAL TEXT: Mircera has been approved for your condition for a 12-week period.

   If no, continue to #4.

4. Is the request for a patient who meets **ALL** of the following?
   - Response to therapy is noted with a rise in hemoglobin of at least 1gm/dL (excludes values due to recent transfusion)
   - Treatment of anemia due to chronic kidney disease
   - Current hemoglobin is less than or equal to 12gm/dL from baseline

   If yes, **approve by HICL for 12 weeks.** Please use status code #057 and the approval text provided.
   APPROVAL TEXT: Mircera has been approved for your condition for a 12-week period.

   If no, do not approve. Please use status code #238 and the denial text provided:
   DENIAL TEXT: Per your health plan's Hematinic Agents guideline, authorization for renewal requires documentation of each of the following:
   - Your current hemoglobin level is less than or equal to 12gm/dL from baseline
   - Your hemoglobin level increased by at least 1gm/dL
   - You are being treated for anemia due to chronic kidney disease

   Your provider did not submit information that you **[meet these conditions or select the specific criteria not met]** and therefore your request was not approved.

CONTINUED ON NEXT PAGE

HEMATINIC AGENTS

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.

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.
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.
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 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 patients not on dialysis.

CONTINUED ON NEXT PAGE

HEMATINIC AGENTS

FDA APPROVED INDICATIONS (CONTINUED)

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 2018.
- Epogen [package insert]. Thousand Oaks, CA: Amgen Inc.; April 2017.
- Procrit [package insert]. Horsham, PA: Janssen Products.; April 2017.
- Retacrit [package insert]. Lake Forest, IL: Hospira Inc,; June 2018.
- National Comprehensive Cancer Network. The NCCN Drugs & Biologics Compendium. http://www.nccn.org. Accessed September 19, 2017.
- Micromedex Solutions [database online]. Ann Arbor, MI: Truven Health Analytics Inc. Updated periodically. www.micromedexsolutions.com [available with subscription]. Accessed September 19, 2017.
- Clinical Consult. Caremark Clinical Programs Review: Focus on Erythropoiesis Stimulating Agents Clinical Programs. July 31, 2007.
- 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, 2017.
- 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 October 16, 2016.
- National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Cancer- and Chemotherapy-Induced Anemia. Version 1.2017. http://www.nccn.org/professionals/physician_gls/pdf/anemia.pdf. Accessed September 19, 2017.
- 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 1.2017. http://www.nccn.org/professionals/physician_gls/pdf/mds.pdf. Accessed September 19, 2017.
- 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 2.2017. https://www.nccn.org/professionals/physician_gls/pdf/mpn.pdf. Accessed September 19, 2017.
- 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.