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Erythropoiesis-Stimulating Agents (ESA's): Epoetin (Epogen[®] and Procrit[®]), and Darbepoetin (Aranesp[®])

Policy # 00210

Original Effective Date: 08/01/2006

Current Effective Date: 05/21/2014

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Epoetin Alfa (Epogen[®] or Procrit[®])[‡] Selection Criteria- Labeled Usage

Patient Selection Criteria

Coverage eligibility will be considered for the use of Epoetin Alfa (Epogen or Procrit) when the following lab criteria are met (unless otherwise specified) and at least one of the clinical criteria listed below is met:

Lab Criteria:

- Hematocrit (Hct)/hemoglobin (Hgb) levels are less than 30%/10g/dL prior to initiation of therapy (not applicable to elective, noncardiac, nonvascular surgery patients); and
- Adequate iron stores with a transferrin saturation of at least 20% and ferritin at least 100ng/ml.

Clinical Criteria:

- Treatment of anemia in cancer patients with non-myeloid malignancies where anemia is due to the effect of concomitantly administered myelosuppressive chemotherapy, and upon initiation, there is a minimum of two additional months of planned chemotherapy (treatment should be discontinued if hemoglobin [Hgb] level exceeds 12g/dl); (*Note: Epoetin Alfa (Epogen or Procrit) is not indicated for patients receiving myelosuppressive therapy when the anticipated outcome is cure*); or
- Treatment of anemia related to therapy with zidovudine (AZT) in human immunodeficiency virus (HIV) infected adults and children (treatment should be discontinued if hemoglobin [Hgb] level exceeds 12g/dl); or
- Treatment of anemia associated with chronic kidney disease (CKD) including patients on dialysis and not on dialysis to decrease the need for red blood cell (RBC) transfusions (treatment should be discontinued if Hematocrit [Hct]/hemoglobin [Hgb] levels exceed 33%/11g/dL); or
- Treatment for surgery patients (hemoglobin [Hgb] >10 to ≤13g/dL) who are scheduled to undergo elective, noncardiac, nonvascular surgery, to reduce the need for allogeneic blood transfusions.

Epoetin Alfa (Epogen or Procrit) Selection Criteria- Off Label Usage

Patient Selection Criteria

Coverage eligibility for the off-label use of Epoetin Alfa will be considered when the following lab criteria are met (unless otherwise specified) and at least one of the clinical criteria listed below is met:



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Lab Criteria:

- Hematocrit (Hct)/hemoglobin (Hgb) levels are less than 30%/10g/dL prior to initiation of therapy (not applicable to anemia patients who donate blood prior to elective surgery); and
- Adequate iron stores with a transferrin saturation of at least 20% and ferritin at least 100ng/ml.

Clinical Criteria:

- To prevent anemia in patients who donate blood and to increase the capacity for donation (for future autologous transfusion) prior to elective surgery ; or
- Treatment of anemia associated with myelodysplastic syndromes in selected patients (treatment should be discontinued if hemoglobin [Hgb] level exceeds 12g/dl); or
- Treatment of anemia in patients with hepatitis C virus infection who are being treated with the combination of ribavirin and interferon alfa or ribavirin and peginterferon alfa or ribavirin and peginterferon alfa with boceprevir or telaprevir (treatment should be discontinued if hemoglobin [Hgb] level exceeds 12g/dl); or
- Treatment of anemia in critically ill patients in hospital intensive care units (treatment should be discontinued if hemoglobin [Hgb] level exceeds 12g/dl).

Note: Epoetin Alfa is not a substitute for blood transfusions, which may be required for the emergency treatment of severe anemia. Chronic use of Epoetin Alfa reduces the need for repeated maintenance blood transfusions.

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of Epoetin Alfa (Epogen or Procrit)[†] for usage not indicated in the patient selection criteria to be **investigational**.*

Based on review of available data, the Company considers the use of Epoetin Alfa (Epogen or Procrit) for non-FDA approved indications and for off-label usage not indicated in the patient selection criteria to be **investigational**.*

Darbepoetin Alfa (Aranesp[®])[†] Selection Criteria

Patient Selection Criteria

Coverage eligibility will be considered for the use of Darbepoetin Alfa (Aranesp)[†] when there is documented failure of Epoetin Alfa (defined as failure to achieve a rise in hemoglobin [Hgb] of 2g/dL or a target hemoglobin [Hgb] of 12g/dL after eight weeks of therapy or significant side effects) for the treatment of anemia in cancer patients and all of the following lab criteria are met and at least one of the clinical criteria listed below is met:

Note: Documented failure of Epoetin Alfa is exempt in the treatment of anemia associated with chronic renal failure.



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Lab Criteria:

- Hematocrit (Hct)/hemoglobin (Hgb) levels are less than 30%/10g/dL prior to initiation of therapy; and
- Adequate iron stores with a transferrin saturation of at least 20% and ferritin at least 100ng/ml.

Clinical Criteria:

- Treatment of anemia in cancer patients with non-myeloid malignancies where anemia is due to the effect of concomitantly administered myelosuppressive chemotherapy, and upon initiation, there is a minimum of two additional months of planned chemotherapy (treatment should be discontinued if Hgb level exceeds 12g/dl); (*Note: Darbepoetin Alfa [Aranesp] is not indicated for patients receiving myelosuppressive therapy when the anticipated outcome is cure*); or
- Treatment of anemia due to chronic kidney disease (CKD), including patients on dialysis and patients not on dialysis (treatment should be discontinued if hematocrit (Hct)/hemoglobin (Hgb) levels exceed 33%/11g/dL).

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of Darbepoetin Alfa (Aranesp) when patient selection criteria are not met [except for the lack of a documented failure of Epoetin Alfa (Epogen or Procrit) when treating anemia in cancer patients which is considered **not medically necessary****] to be **investigational.***

Based on review of available data, the Company considers the use of Darbepoetin Alfa (Aranesp) for non-FDA approved indications to be **investigational.***

When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the use of Darbepoetin Alfa (Aranesp) when there is no documented failure of Epoetin Alfa (Epogen or Procrit) when treating anemia in cancer patients to be **not medically necessary.****

Background/Overview

Erythropoietin (EPO) is a glycoprotein which stimulates RBC production. It is produced in the kidney and is secreted when the kidneys detect changes in oxygen levels. Low levels of EPO can lead to significant anemia. Plasma EPO levels remain constant (2 to 40mU/mL) when Hgb levels remain ≥ 12 g/dL but rise rapidly when Hgb drops below this level. It takes four to seven days following EPO stimulation for mature RBCs to be released. In patients with decreased renal function and decreased renal EPO production, the kidneys are not able to respond to the hypoxia by producing more EPO.

Two hematopoietic growth factors are currently available in the United States; Epoetin Alfa and Darbepoetin Alfa.



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Epoetin Alfa, a 165 amino acid glycoprotein manufactured by recombinant deoxyribonucleic acid (DNA) technology, has the same biological effects as endogenous EPO. It has a molecular weight of 30,400 daltons and is produced by mammalian cells into which the human EPO gene has been introduced. The product contains the identical amino acid sequence of isolated natural EPO.

Darbepoetin Alfa is an erythropoiesis stimulating protein, closely related to EPO that is produced in Chinese hamster ovary (CHO) cells by recombinant DNA technology. Aranesp is a 165-amino acid protein that differs from recombinant human erythropoietin (rHuEPO) in containing five N-linked oligosaccharide chains, whereas rHuEPO contains three chains. The two additional N-glycosylation sites result from amino acid substitutions in the EPO peptide backbone. The additional carbohydrate chains increase the approximate molecular weight of the glycoprotein from 30,000 to 37,000 daltons.

Epoetin Alfa and Darbepoetin Alfa are formulated as sterile, colorless liquid solutions for intravenous (IV) or subcutaneous (SC) administration.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Two ESA products have been licensed in the U.S. Epoetin alfa is manufactured, distributed, and marketed by Amgen, Inc. under the proprietary name, Epogen. The same epoetin alfa product manufactured by Amgen, Inc. is also marketed and distributed by Janssen Products, LP, a subsidiary of Johnson and Johnson, under the proprietary name, Procrit. Under a contractual agreement with Amgen, Janssen Products, LP has rights to development and marketing of Procrit for any indication other than for the treatment of anemia associated with chronic renal failure in patients on dialysis or use in diagnostic test kits. Epogen and Procrit have identical labeling information for all FDA-approved indications. A second ESA, darbepoetin alfa, is marketed solely by Amgen, under the proprietary name, Aranesp.

The epoetin alfas have the same amino acid sequence as endogenous EPO, while darbepoetin alfa has 2 additional oligosaccharide chains. In contrast, peginesatide lacks any amino acid sequence homology to EPO. It is a synthetic dimer of identical 21-amino acid peptides bound to a linker and to polyethylene glycol, with a total molecular weight of approximately 45,000 daltons. However, the epoetins, darbepoetin, and peginesatide all have pharmacologic actions similar to those of the endogenous hormone. Each binds to and activates the human EPO receptor and thus increases the number of RBCs and the blood concentration of hemoglobin, when given to individuals with functioning erythropoiesis. All currently marketed ESAs are approved as treatment of anemia associated with CKD in adult patients on dialysis. The two epoetin alfas and darbepoetin are also approved to treat pediatric patients on dialysis with anemia from CKD, anemic patients with CKD not on dialysis, and for other indications.

The major regulatory timelines for approval actions pertaining to new indications is summarized below:

Epoetin alfa (Epogen/Procrit):

- 1989: approved for use among anemic CRF patients
- 1991: approved for use among AZT-treated HIV-infected patients
- 1993: approved for use for chemotherapy-induced anemia among patients with non-myeloid malignancies

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- 1996: approved for presurgical use among certain patients undergoing surgery

Darbepoetin alfa (Aranesp):

- 2001: approved for use among anemic CRF patients
- 2002: approved for use for chemotherapy-induced anemia among patients with non-myeloid malignancies

Centers for Medicare and Medicaid Services (CMS) Postapproval Decision Memorandum

In July 2007, CMS released a Decision Memorandum on the use of ESAs for non-renal disease indications (CAG-00383N). Safety concerns such as thrombosis, cardiovascular events, tumor progression, and reduced survival, derived from clinical trials in several cancer and non-cancer populations, prompted CMS to review its coverage of ESAs. The CMS reviewed a large volume of scientific literature, including basic science research, to see if safety findings observed in RCTs could be reasonably explained in whole or in part by the actions of ESAs on normal or cancerous cells. Based on this review, CMS proposed conditions of coverage based on expression of EPO receptors. However, the scientific understanding of this mechanism is controversial and requires additional study.

The CMS also reviewed comments on ESAs treatment of myelodysplastic syndrome (MDS), a precursor of acute myeloid leukemia (AML) in many patients. The CMS retains interest in these specific issues but does not differentiate ESA coverage by the EPO receptor status of the underlying disease and has decided to make no national coverage determination (NCD) at this time on ESAs in MDS.

The CMS has determined that evidence is sufficient to conclude that ESA treatment is not reasonable and necessary for beneficiaries with certain clinical conditions, either because of a deleterious effect of the ESA on their underlying disease or because the underlying disease increases their risk of adverse effects related to ESA use. These conditions include:

- Any anemia in cancer or cancer treatment patients due to folate deficiency, B-12 deficiency, iron deficiency, hemolysis, bleeding, or bone marrow fibrosis
- Any anemia associated with the treatment of acute and chronic myelogenous leukemias (CML, AML), or erythroid cancers
- Anemia of cancer not related to cancer treatment
- Any anemia associated only with radiotherapy
- Prophylactic use to prevent chemotherapy-induced anemia
- Prophylactic use to reduce tumor hypoxia
- Patients with EPO-type resistance due to neutralizing antibodies
- Anemia due to cancer treatment if patients have uncontrolled hypertension.

The CMS also determined that ESA treatment for the anemia secondary to myelosuppressive anticancer chemotherapy in solid tumors, multiple myeloma, lymphoma and lymphocytic leukemia is only reasonable and necessary under the following specified conditions:

- The hemoglobin level immediately prior to initiation or maintenance of ESA treatment is < 10 g/dL (or the hematocrit is < 30%).



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- The starting dose for ESA treatment is the recommended FDA label starting dose, no more than 150U/kg/3 times weekly for epoetin and 2.25mcg/kg/weekly for darbepoetin alpha. Equivalent doses may be given over other approved time periods.
- Maintenance of ESA therapy is the starting dose if the hemoglobin level remains below 10g/dL (or hematocrit is < 30%) 4 weeks after initiation of therapy and the rise in hemoglobin is > 1g/dL (hematocrit > 3%).
- For patients whose hemoglobin rises < 1g/dL (hematocrit rise < 3%) compared to pretreatment baseline over 4 weeks of treatment and whose hemoglobin level remains < 10g/dL after the 4 weeks of treatment (or the hematocrit is < 30%), the recommended FDA label starting dose may be increased once by 25%. Continued use of the drug is not reasonable and necessary if the hemoglobin rises < 1g/dL (hematocrit rise < 3%) compared to pretreatment baseline by 8 weeks of treatment.
- Continued administration of the drug is not reasonable and necessary if there is a rapid rise in hemoglobin > 1g/dL (hematocrit > 3%) over 2 weeks of treatment unless the hemoglobin remains below or subsequently falls to < 10 g/dL (or the hematocrit is < 30%). Continuation and reinstitution of ESA therapy must include a dose reduction of 25% from the previously administered dose.
- ESA treatment duration for each course of chemotherapy includes the 8 weeks following the final dose of myelosuppressive chemotherapy in a chemotherapy regimen.

This decision by CMS also allows local Medicare contractors to continue to make reasonable and necessary determinations on all uses of ESAs that are not determined by NCD.

Rationale/Source

Chronic Kidney Disease

Chronic kidney disease is the clinical situation in which there is a progressive and usually irreversible decline in kidney function. Such patients may manifest the sequelae of renal dysfunction, including anemia, but do not necessarily require regular dialysis. Patients with end-stage renal disease (ESRD) are those patients with CKD who require regular dialysis or kidney transplantation for survival.

Chronic kidney disease patients can frequently experience anemia, which can significantly affect their morbidity, mortality and quality of life. rHuEPO is effective for the treatment of anemia in CKD based on its ability to increase hemoglobin, virtually eliminate the need for RBC transfusions, mitigate symptoms associated with anemia and improve energy and physical functioning.

The National Kidney Foundation Kidney Disease Outcome Quality Initiative (NKF-K/DOQI) practice guidelines for anemia of CKD, updated in 2000, state that the target Hgb range for EPO therapy is 11.0g/dL to 12.0g/dL.³ The European Best Practice Guidelines for the management of anemia in CRF patients, published in 2004, state that EPO agents should be given to all patients with CKD with a Hgb below 11.0g/dL.⁴ The criterion of requiring a Hgb $\leq$ 11.0g/dL is recommended based on the professional opinion of specialized physicians. *Note: patients previously receiving other similar recombinant EPOs (darbepoetin) and switching to epoetin alfa, or who have been maintained on epoetin alfa, are not required to have Hgb 11.0g/dL.*



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AZT-treated HIV-infected Patients

Response to EPO therapy in AZT-treated HIV-infected patients is manifested by reduced transfusion requirements and increased Hct.

Cancer Patients on Chemotherapy

Chemotherapy-induced anemia has debilitating effects on patients with cancer. Epoetin Alfa and Darbepoetin Alfa are growth factors that stimulate RBC formation and are approved and widely adopted for the management of chemotherapy-induced anemia.

Clinical evidence exists showing that epoetin alfa is well tolerated and highly effective at increasing Hgb and decreasing transfusion requirements in anemic patients with cancer.

Though molecularly distinct from Epoetin Alfa, Darbepoetin Alfa binds to the same EPO receptor and stimulates erythropoiesis by the same mechanism. Clinical trials in anemic patients with cancer receiving chemotherapy have demonstrated that Darbepoetin Alfa also is effective in raising Hgb levels and reducing transfusion requirements.

The Agency for Healthcare Research and Quality (AHRQ) study reported in 2006 has shown that Epoetin Alfa and Darbepoetin Alfa are therapeutically equivalent in chemotherapy-induced anemia.

The dose conversion ratio (DCR) of 330:1 estimated for the 2004 Hospital Outpatient Prospective Payment System by the Centers for Medicare and Medicaid Services is greater than the DCRs estimated based on HbAUC. The DCR estimated in the primary regression suggest that based on average wholesale prices (AWPs), EPO is 2.0 times more cost effective than DARB.

A DCR is defined as the ratio of doses at which two agents are equally effective. A DCR is assessed by either the mean weekly dose to mean cumulative dose for each erythropoietic agent divided by the effect, or area under the curve of Hgb change for each agent.

2007 FDA Alert

The product information labels for Darbepoetin Alfa (Aranesp), and Epoetin Alfa (Epogen and Procrit), have recently been updated and are summarized here:

A New Boxed Warning providing the following information:

- Renal Failure: Patients experienced greater risk for death and serious cardiovascular events when administered ESAs to target higher versus lower Hgb levels (13.5 vs 11.3g/dL; 14 vs 10g/dL) in two clinical studies. Individualize dosing to achieve and maintain Hgb levels with range of 10 to 12g/dL.
- Cancer:
 - o ESAs shortened overall survival and/or time-to-tumor progression in clinical studies in patients with advanced breast, head and neck, lymphoid and non-small cell lung malignancies when dosed to target Hgb of ≥ 12 g/dL.



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- o The risks of shortened survival and tumor progression have not been excluded when ESAs are dosed to target an Hgb of < 12g/dL.
 - o To minimize these risks, as well as the risk of serious cardio-and thrombovascular events, use the lowest dose needed to avoid RBC transfusions.
 - o Use only for treatment of anemia due to concomitant myelosuppressive chemotherapy.
 - o Discontinue following the completion of a chemotherapy course.
- Perisurgery: Procrit/Epogen increased the rate of deep venous thromboses in patients not receiving prophylactic anticoagulation. Consider deep venous thrombosis prophylaxis. (*Note: Aranesp is not approved for this indication*).

Additional Warnings about increased mortality, cardiovascular events, tumor progression and uncontrolled hypertension

- Increased Mortality and Cardiovascular Events – the warnings now describe the results of new studies showing an increased incidence of thrombotic events in patients with chronic renal failure, cancer patients on chemotherapy and surgical candidates.
- Potential for Tumor Growth Progression– a new subsection in Warnings describes the new data and emphasizes the evidence for increased rate of tumor progression.
- Hypertension–this subsection advises against the use of ESAs in patients with uncontrolled hypertension, and describes the risks to and guidance for managing controlled hypertensive patients.

Recommendations and Considerations

Physicians and other healthcare professionals should consider the following when using ESAs:

For all patients:

- Use the lowest dose possible to gradually increase the Hgb concentration to avoid the need for transfusion.
- Measure Hgb twice a week for two to six weeks after any dosage adjustment to ensure that Hgb has stabilized in response to the dose change.
- Withhold the dose of the ESA if the Hgb increase exceeds 12g/dL or rises by 1g/dL in any two week period.

For cancer patients:

- Use of an ESA in anemic cancer patients who are not on chemotherapy offered no benefit and may shorten the time to death.
- ESAs are not-FDA approved to treat anemia in cancer patients not receiving chemotherapy
- There is a potential risk of shortening the time to tumor progression or disease-free survival
- ESAs are administered only to avoid RBC transfusions in cancer patients. ESAs do not improve the outcome of cancer treatment and do not alleviate fatigue or increase energy.

FDA Dosing and Monitoring Recommendations

For CRF patients:

- Measure Hgb twice a week after initiating treatment until Hgb has stabilized

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For cancer patients and AZT-treated HIV patients:

- Measure Hgb once a week after initiating treatment until Hgb has stabilized

For patients with a history of cardiovascular disease or hypertension:

- Closely monitor and control blood pressure

2008 FDA Alert

FDA informed healthcare professionals of modifications to certain sections of the Boxed Warnings, Indications and Usage, and Dosage and Administration sections of prescribing information for ESAs. The changes clarify the FDA-approved conditions for use of ESAs in patients with cancer and revise directions for dosing to state the hemoglobin level at which treatment with an ESA should be initiated. Additional revisions to prescribing information that ESAs are not intended for use in receiving myelosuppressive therapy when the expected outcome is cure and when to initiate and discontinue ESA dosing will be forthcoming. FDA continues to encourage healthcare professionals to discuss with their patients before starting or continuing therapy with ESAs, the benefits of treatment with ESAs and the potential and demonstrated risks of ESAs for thrombovascular events, shortened time to tumor progression or recurrence and shortened survival time.

FDA Medwatch. The FDA Safety Information and Adverse Event Reporting Program. July 30, 2008.

2011 FDA Alert

The FDA has modified their recommendations for more conservative dosing of ESA in patients with CKD to improve the safe use of these drugs.

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Coding

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Codes used to identify services associated with this policy may include (but may not be limited to) the following:

Code Type	Code
CPT	No codes
HCPCS	J0881, J0882, J0885, J0886, J0890, Q4081
ICD-9 Diagnosis	042, 070.44, 070.54, 238.71 thru 238.75, 285.9, 585.1 thru 585.9, V42.81 thru V42.82
ICD-9 Procedure	99.29

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07/12/2006 Medical Director review
07/19/2006 Medical Policy Committee approval
07/10/2007 Medical Director review
07/18/2007 Medical Policy Committee approval. FDA box warning, lab criteria and the use of Epoetin alpha and Darbepoetin alfa when hgb exceeds 12g/dL is considered not medically necessary was added.
09/03/2008 Medical Director review
10/22/2008 Medical Policy Committee approval. Clinical criteria changed to reflect coverage is only when a cure is not the anticipated outcome in patients with non myeloid malignancies with anemia. New FDA black box warning update added to rationale.
12/04/2009 Medical Policy Committee approval.
12/16/2009 Medical Policy Implementation Committee approval. Changed title from Recombinant Human Erythropoietin: Epoetin (Epogen® and Procrit®) and Darbepoetin (Aranesp®) to Erythropoiesis-Stimulating Agents (ESA's): Epoetin (Epogen® and Procrit®) and Darbepoetin (Aranesp®). When Services Are Considered Not Medically Necessary and/or Excluded from Coverage verbiage deleted from the policy. Added an investigational statement for Epoetin Alfa usage for non-FDA approved indications and for off-label usage not indicated in the patient selection criteria. Added investigational statements for Darbepoetin Alfa usage when patient selection criteria are not met

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	and for usage for non-FDA approved indications. Added a third bullet for Epoetin Alfa lab criteria that a target hemoglobin of $\leq 12\text{g/dL}$ is indicated for all labeled and off-labeled usage.
12/01/2010	Medical Policy Committee approval.
12/15/2010	Medical Policy Implementation Committee approval. No change to coverage.
07/07/2011	Medical Policy Committee approval.
07/20/2011	Medical Policy Implementation Committee approval. Lab values for chronic renal failure was changed to Hct/Hgb levels are less than 30%/10 g/dl prior to initiation of therapy. Added, "or ribavirin and peginterferon alfa with boceprevir or telaprevir" to the third criteria bullet for Epoetin Alfa Selection Criteria- Off Label Usage.
08/19/2011	"Discontinue treatment if (Hct/Hgb levels exceeds $\geq 33\%/11\text{g/dL}$ " was added to chronic renal failure patients criteria. "For all labeled usage, a target hemoglobin of $\leq 12\text{g/dL}$ is indicated and should not be exceeded for maintenance or recurrent use" was removed from policy.
05/03/2012	Medical Policy Committee approval.
05/16/2012	Medical Policy Implementation Committee approval. New FDA approved drug Omontys added to the policy. Hgb level as to when to stop therapy has been changed to >11 to match ESI call tree.
02/04/2013	Coding update
05/02/2013	Medical Policy Committee review
05/22/2013	Medical Policy Implementation Committee approval. Clarified that the lack of use of Epogen/Procrit prior to Aranesp in cancer patients is Not Medically Necessary. Aesthetic changes throughout. Language clarified to match Pharmacy call tree. No coverage changes.
05/01/2014	Medical Policy Committee review
05/21/2014	Medical Policy Implementation Committee approval. Removed Omontys from policy.
Next Scheduled Review Date:	05/2015

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

- A. whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
- B. whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
 1. Consultation with the Blue Cross and Blue Shield Association technology assessment program (TEC) or other nonaffiliated technology evaluation center(s);
 2. credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
 3. reference to federal regulations.

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

- A. in accordance with nationally accepted standards of medical practice;
- B. clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
- C. not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

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Erythropoiesis Stimulating Agents (ESA's): Epoetin (Epogen[®] and Procrit[®]), and Darbepoetin (Aranesp[®])

Policy # 00210

Original Effective Date: 08/01/2006

Current Effective Date: 05/21/2014

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

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