

LCD for Erythropoiesis Stimulating Agents (L26655)

Contractor Information

Contractor Name

Wisconsin Physicians Service Insurance Corporation

Contractor Number

05101, 05201, 05301, 05401, 05102, 05202, 05302, 05402

Contractor Type

MAC

LCD Information

LCD ID Number

L26655

LCD Title

Erythropoiesis Stimulating Agents

Contractor's Determination Number

INJ-523

AMA CPT / ADA CDT Copyright Statement

CPT codes, descriptions and other data only are copyright 2009 American Medical Association (or such other date of publication of CPT). All Rights Reserved. Applicable FARS/DFARS Clauses Apply. Current Dental Terminology, (CDT) (including procedure codes, nomenclature, descriptors and other data contained therein) is copyright by the American Dental Association. © 2002, 2004 American Dental Association. All rights reserved. Applicable FARS/DFARS apply.

CMS National Coverage Policy

CMS National Coverage Policy Related to Erythropoietin Analogues

NCDs and coverage provisions in interpretive manuals are not subject to the LCD Review Process (42 CFR 405.860[b] and 42 CFR 426 [Subpart D]). In addition, an administrative law judge may not review an NCD. See §1869(f)(1)(A)(i) of the Social Security Act.

Title XVIII of the Social Security Act (SSA):

Section 1833(e) prohibits Medicare payment for any claim which lacks the necessary information to process the claim.

Section 1862(a)(1)(A) excludes expenses incurred for items or services which are not reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member.

Section 1862(a)(7) excludes routine physical examination.

Section 1881(b)(1) allows payment for services furnished to individuals who have been determined to have end stage renal disease.

Section 1881(11)(B)(I) allows payment for erythropoietin provided by a physician.

CMS Publications:

CMS Publication 100-02, Medicare Benefit Policy Manual, Chapter 1:
30 Drugs and Biologicals

CMS Publication 100-02, Medicare Benefit Policy Manual, Chapter 6:
30 Drugs and Biologicals

CMS Publication 100-02, Medicare Benefit Policy Manual, Chapter 11:
30.1 Frequency of Dialysis Sessions
30.4 Drugs and Biologicals
30.5 New ESRD Composite Payment Rates Effective January 1, 2005
90 Epoetin (EPO)

CMS Publication 100-02, Medicare Benefit Policy Manual, Chapter 15:
50 Drugs and Biologicals
50.1 Definition of Drug or Biological
50.2 Determining Self-Administration of Drug or Biological
50.3 Incident-to Requirements
50.4.1 Approved Use of Drug
50.4.3 Examples of Not Reasonable and Necessary
50.5.2 Erythropoietin (EPO)
50.5.2.1 Requirements for Medicare Coverage for EPO [home use]
50.5.2.2 Medicare Coverage of Epoetin Alfa (Procrit) for Preoperative Use

CMS Publication 100-04, Medicare Claims Processing Manual, Chapter 6:
10.1 Consolidated Billing Requirement for SNFs
20.2 Services Excluded from Part A PPS Payment
20.2.1.1 ESRD Services
20.2.1.4 Coding Applicable to EPO Services

CMS Publication 100-04, Medicare Claims Processing Manual, Chapter 8:
10.5 Hospital Services
60.4 Separately Billable ESRD Items and Services – Erythropoietin
60.4.1 Epoetin Alfa (EPO) Facility Billing Requirements
60.4.3 Payment Amount for Epoetin Alfa (EPO)
60.4.3.2 Epoetin Alfa (EPO) Provided in the Hospital Outpatient Department
60.7 Darbepoetin Alfa (Aranesp (R)) for ESRD Patients
60.7.1 Darbepoetin Alfa (Aranesp (R)) Facility Billing Requirements Using UB-92/Form CMS-1450
60.7.3 Payment Amount for Darbepoetin Alfa (Aranesp(R))
60.7.4
60.7.3.2 Payment for Darbepoetin Alfa (Aranesp(R)) in the Hospital Outpatient Department
80.2.1 Required Billing Information for Method I Claims
90 Method II Billing
90.5 Method II Support Services Billed to the Intermediary by the Facility
90.5.1 Billable UB-92 Revenue Codes Under Method II
90.5.1.1 Unbillable UB-92 Revenue Codes Under Method II

CMS Publication 100-04, Medicare Claims Processing Manual, Chapter 17:
Drugs and Biologicals 10; 80.5 (Rev.1412, 01-11-08)
Section 10 Payment Rules for Drugs and Biologicals
Section 20.5.8 Injections Furnished to ESRD Beneficiaries

CMS Publication 100-04, Medicare Claims Processing Manual, Chapter 25:
Section 60 General Instructions for Completion of Form CMS-1450 for Billing

CMS Publication 100-04, Medicare Claims Processing Manual, Chapter 27:
Section 80.8 ESRD Maintenance Transaction Error Codes.

CMS Publication 100-04, Medicare Claims Processing Manual, Transmittal No. 1212, Change Request #5480, March 30, 2007, 2005, Requirement for Providing route of administration codes for Erythropoiesis stimulating agents (ESAs).

CMS Publication 100-04, Medicare Claims Processing Manual, Transmittal No. 1041, Change Request #5216, August 25, 2006, confirms that hospitals are to continue to report administration of epoetin alfa using revenue codes 634 and 635 and replaces HCPCS code J0886 with Q4081 for bill types 12X, 13X, 72X, and 85X for dates of service on or after 01/01/2007.

CMS Publication 100-04, Medicare Claims Processing Manual, Transmittal No. 1043, Change Request #5251, August 25, 2006, revises the definition of the GS modifier.

CMS Publication 100-04, Medicare Claims Processing Manual, Transmittal No. 751, Change Request #4135, November 10, 2005, describes a new national monitoring policy for EPO and Aranesp(R) for ESRD patients treated in renal dialysis facilities.

CMS Publication 100-04, Medicare Claims Processing Manual, Transmittal No. 737, Change Request #4108, October 31, 2005, provides updated HCPCS codes for epoetin alfa and darbepoetin alfa.

CMS Publication 100-04, Medicare Claims Processing Manual, Transmittal No. 736, Change Request #4103, October 31, 2005, re-defines value code 49 and provides revenue coding instructions for bill type 12X.

CMS Publication 100.04, Medicare Claims Processing Manual, Transmittal No. 1285, Change Request #5545, July 13, 2007, completes the implementation of ESRD line item billing for Renal Dialysis Facilities by providing instructions required to submit line item billing EPO on ESRD claims.

CMS Publication 100.04, Medicare Claims Processing Manual, Transmittal NO. 1307, Change Request # 5700, July 20, 2007, Modification to the National Monitoring Policy for Erythropoietic Stimulating Agents (ESAs) for End-Stage Renal Disease (ESRD) Patients Treated in Renal Dialysis Facilities

Tax Relief and Health Care Act of 2006 Section 110 of Division B directs the Secretary to amend Section 1842 of the Social Security Act by adding at the end the following new subsection: "(u) Each request for payment, or bill submitted, for a drug furnished to an individual for the treatment of anemia in connection with the treatment of cancer shall include (in a form and manner specified by the Secretary) information on the hemoglobin or hematocrit levels for the individual."

One Time Notifications:

Pub. 100-20, Transmittal: 19; 11/7/2003; CR 2984

Pub. 100-20, Transmittal: 18; 10/31/2003; CR 2963

Pub. 100-20, Transmittal: 36; 12/24/2003; CR 3037

Formerly

MCM 2049.5, 2050.5, 4273.1B, 5202.3, 5202.4

Program Memorandums: BPO-B22 (07/19/93); IL 08/24/94; C012/B5202.4/EPOCLAR; B-95-2, 05/25/95; PM Rev. AB-97-2, 02/13/97; PM Rev. AB-97-12, 08/97; PM AB-98-10, 03/98; PM AB-98-34 07/98; CMS memo 01/22/99; AB-99-59, 08/99; AB-02-100, CR 2266, 5/24/2002; 2003 HCPCS update, 11/2002; AB-03-135 CR2630, 08/26/03, AB-03-062, 05/02/2003

Oversight Region

Region I

Original Determination Effective Date

For services performed on or after 02/01/2008

Original Determination Ending Date**Revision Effective Date**

For services performed on or after 11/16/2009

Revision Ending Date**Indications and Limitations of Coverage and/or Medical Necessity**

Naturally occurring human erythropoietin is a glycoprotein produced mainly in the kidneys. It stimulates the division and differentiation of committed erythroid progenitors in bone marrow. A number of chronic conditions, especially chronic renal failure, result in decreased production of erythropoietin, often causing anemia. Supplementation by synthetic drugs with structures identical or similar to naturally occurring erythropoietin has been proven safe and effective in correcting anemia in certain groups of patients. Normal plasma erythropoietin levels may vary from 0.01 to 0.03 U/ml (10-30 MU/ml). These levels may increase 100 to 1000 - fold during hypoxia or anemia, and one may see levels from 1,000 to 30,000 MU/ml. Certain conditions blunt this normal physiological response to anemia and so erythropoietin levels do not rise. This causes or aggravates anemia. Anemia of chronic renal failure, as well as certain other anemias, despite adequate erythropoietin levels, may respond to supplemental erythropoietin administration.

There are rare patients whose cardiac, pulmonary or other medical diseases warrant the use of ESAs to maintain a hemoglobin/hematocrit (Hgb/HCT) higher than the target level discussed in this LCD. Documentation to support this practice must be available upon request. This does not apply to ESA therapy for anemia related to cancer chemotherapy, which follows the rules mandated by the National Coverage Decision.

During therapy virtually all patients will eventually require supplemental iron. Stores of iron should be regularly monitored to insure transferrin saturation at or above 20% and/or serum ferritin levels at or greater than 100mg/ml, in order to guide appropriate supplementation.

The FDA has approved two distinct drugs for use as synthetic erythropoietin substitutes.

1. Epoetin alfa (EPO) is a biologically engineered protein, which stimulates the bone marrow to make new red blood cells. EPO is a glycoprotein, produced by recombinant DNA technology. Recombinant EPO has the same biological activity as the endogenous hormone, which induces erythropoiesis by stimulating the division and differentiation of committed erythroid progenitor cells in bone marrow.

2. Darbepoetin alfa (DPA) is a supersialated protein that binds to the erythropoietin receptor and stimulates erythropoiesis by the same mechanism as endogenous erythropoietin. It has a half-life approximately two to three times longer than Epoetin alfa and therefore needs to be administered less often.

The following causes of anemia should be considered, documented, and corrected (when possible) before starting therapy:

- iron deficiency;
- underlying infection or inflammatory process;
- underlying hematological disease;
- hemolysis;
- vitamin deficiencies (e.g. folic acid or B 12);
- blood loss;
- aluminum intoxication.
- drug exposure history

Therefore prior to therapy, the physician makes a comprehensive assessment of the patient, which would include:

1. Hematocrit or hemoglobin
2. Serum iron
3. Transferrin saturation; or serum ferritin and /or documentation of iron stores in bone marrow
4. Creatinine
5. Bone Marrow Biopsy (for myelodysplastic disease or where otherwise indicated)
6. Erythropoietin level (for myelodysplastic disease; AZT therapy, anemia of chronic disease)

Contraindications

ESAs are contraindicated in patients with:

1. Uncontrolled hypertension.
2. Known hypersensitivity to mammalian cell-derived products.
3. Known hypersensitivity to Albumin (Human).

Warnings

Adults

1. Mortality, Cardiovascular Events and Hemoglobin Levels

Erythropoietic therapies may increase the risk of cardiovascular events, including death. The higher risks of cardiovascular events may be associated with higher hemoglobin and/or higher rates of rise of hemoglobin. Target hemoglobin levels should not exceed 12g/dL.

2. Pure Red Cell Aplasia

Cases of pure red cell aplasia (PRCA) and of severe anemia, with or without other cytopenias, associated with neutralizing antibodies to erythropoietin, have been reported in patients treated with erythropoietic therapy. This has been reported predominantly in patients with CRF receiving the drug(s) by subcutaneous administration.

3. Albumin (Human)

Erythropoietic drugs contain albumin, a derivative of human blood. Based on effective donor screening and product manufacturing processes, it carries an extremely remote risk for transmission of viral diseases. A theoretical risk for transmission of Creutzfeldt- Jakob disease (CJD) also is considered extremely remote. No cases of transmission of viral diseases or CJD have ever been identified for albumin.

Chronic Renal Failure Patients

4. Hypertension: Patients with uncontrolled hypertension should not be treated with erythropoietin; blood pressure should be controlled adequately before initiation of therapy. Special care should be taken to closely monitor and aggressively control blood pressure in these patients.

It is recommended that the dose of these agents be decreased if the hemoglobin increase exceeds 1 g/dL in any 2-week period, because of the possible association of excessive rate of rise of hemoglobin with an exacerbation of hypertension.

5. Seizures: Seizures have occurred in patients with CRF participating in clinical trials.

Given the potential for an increased risk of seizures during the first 90 days of therapy, blood pressure and the presence of premonitory neurologic symptoms should be monitored closely. Patients should be cautioned to avoid potentially hazardous activities such as driving or operating heavy machinery during this period.

While the relationship between seizures and the rate of rise of hemoglobin is uncertain, it is recommended that the dose of the Erythropoietin Stimulating Agent (ESA) should be decreased if the hemoglobin increase exceeds 1 g/dL in any 2-week period.

6. Thrombotic Events: During hemodialysis, patients treated with ESAs may require increased anticoagulation with heparin to prevent clotting of the artificial kidney. Other thrombotic events (eg, myocardial infarction, cerebrovascular accident, transient ischemic attack) have occurred in clinical trials at an annualized rate of less than 0.04 events per patient year of therapy.

Also, prior to elective surgery, for the purposes of reducing the requirements for allogeneic blood transfusion, the patient should receive adequate antithrombotic prophylaxis in order to reduce the incidence of deep venous thrombosis.

Consideration should be given to minimize use of ESAs in patients with high risk of thromboembolic events.

Lack or Loss of Response

Because of the length of time required for erythropoiesis (several days for erythroid progenitors to mature and be released into the circulation) a clinically significant increase in hematocrit is usually not observed in less than 2 weeks and may require up to six weeks in some patients.

If the patient fails to respond or to maintain a response to doses within the recommended dosing range, the following etiologies should be considered and evaluated:

1. Iron deficiency: Virtually all patients will eventually require supplemental iron therapy.

Iron Evaluation

During ESAtreatment, absolute or functional iron deficiency may develop. Functional iron deficiency, with normal ferritin levels but low transferrin saturation, is presumably due to the inability to mobilize iron stores rapidly enough to support increased erythropoiesis. Transferrin saturation should be at least 20% and ferritin should be at least 100 ng/mL. Prior to and during therapy, the patient's iron status, including transferrin saturation (serum iron divided by iron binding capacity) and serum ferritin, should be evaluated. Virtually all patients will eventually require supplemental iron to increase or maintain transferrin saturation to levels which will adequately support erythropoiesis stimulated by this therapy. All surgery patients being treated with an ESA should receive adequate iron supplementation throughout the course of therapy in order to support erythropoiesis and avoid depletion of iron stores.

2. Underlying infectious, inflammatory, or malignant processes.

3. Occult blood loss.

4. Underlying hematologic diseases (ie, thalassemia, refractory anemia, or other myelodysplastic disorders).

5. Vitamin deficiencies: Folic acid or vitamin B12.

6. Hemolysis.

7. Aluminum intoxication.

8. Osteitis fibrosa cystica.

9. Pure Red Cell Aplasia (PRCA) or anti-erythropoietin antibody-associated anemia: In the absence of another etiology, the patient should be evaluated for evidence of PRCA and sera should be tested for the presence of antibodies to erythropoietin.

Indications:

Erythropoietin analogues are covered to treat patients who have one of the FDA-approved or "accepted" conditions, and have either symptomatic anemia or are transfusion dependent.

An unlabeled use of a drug is a use that is not included as an indication on the drug's label as approved by the FDA. FDA approved drugs used for indications other than what is indicated on the official label may be covered under Medicare if the carrier determines the use to be medically accepted, taking into consideration the major drug compendia, authoritative medical literature and/or accepted standards of medical practice. In the case of drugs used in an anti-cancer chemotherapeutic regimen, unlabeled uses are covered for a medically accepted indication as defined in §50.4.5. (CMS Publication 100-02, Medicare Benefit Policy Manual, Chapter 15, §50.4.2).

Determinations as to whether medication is reasonable and necessary for an individual patient should be made on the same basis as all other such determinations (i.e., with the advice of medical consultants and with reference to accepted standards of medical practice and the medical circumstances of the individual case) (CMS Publication 100-02, Medicare Benefit Policy Manual, Chapter 15, §50.4.3).

1. Titrate the dose of ESA that will gradually increase the hemoglobin concentration to the lowest level sufficient to avoid blood transfusion
2. Realize that raising the hemoglobin level to greater than 12 increases the risk for cardiovascular events.
3. Realize that there has been reported a higher incidence of deep vein thrombosis in patients receiving epoetin preop to avoid blood transfusion.

Dosage of EPO and DPA: Dosage is based on body weight and can vary among different disease entities (e.g., cancer vs. renal failure.) The dosage, frequency and duration of treatment should not exceed the accepted standards of practice for the covered condition. The dosages are titrated to achieve a consistent Hgb/HCT level.

Initiation of Therapy

Initiation of therapy may begin with a HCT of 30% or HGB of 10 or less. If the transferrin saturation is less than 20% and the serum ferritin is less than 100mg/ml, appropriate iron supplementation should be administered.

Maintenance therapy

Effective 04/16/2008 the maintenance hematocrit level should be maintained at 30-36 or the Hemoglobin (Hgb) level should be maintained at 10-12.

Use the lowest dose of ESA that will gradually increase the hemoglobin concentration to the lowest level sufficient to avoid the need for red blood cell transfusion.

1. For darbepoetin alfa (DPA) and epoetin alpha the manufacturer provides this language: "titrate as necessary to maintain a target Hb not to exceed 12g/dl". This translates to a hematocrit at or around 36. Therefore, we would not expect utilization of EPO or DPA when Hgb/Hct levels were persistently above 12/36 respectively.

2. Follow-up treatment should include an evaluation of effectiveness and continued necessity for EPO and DPA, including the patient's hematocrit.

3. Increases in dose should not be made more frequently than once a month. If the hemoglobin is increasing and approaching 12 g/dL, the dose should be reduced by approximately 25%. If the hemoglobin continues to increase, dose should be temporarily withheld until the hemoglobin begins to decrease, at which point therapy should be reinitiated at a dose approximately 25% below the previous dose. If the hemoglobin increases by more than 1 g/dL in a 2-week period, the dose should be decreased by approximately 25%.

If the increase in the hemoglobin is less than 1 g/dL over 4 weeks and iron stores are adequate, the dose may be increased by approximately 25% of the previous dose. Further increases may be made at 4-week intervals until the specified hemoglobin is obtained.

B. Epoetin alpha (EPO) and darbepoetin alfa (DPA) may be a covered service for treatment of anemia when other treatable causes of anemia are identified and treated and when the anemia is associated with the following conditions:

1. Patients with End Stage Renal Disease (ESRD) on dialysis and those with chronic renal failure not on dialysis.

The likelihood of anemia associated with EPO deficiency increases as renal failure progresses, because the diseased kidneys are unable to produce sufficient quantities of erythropoietin. The anemia of Chronic Renal Failure should not be confused with the anemia of chronic disease. In the latter, inflammatory cytokines suppress the endogenous production of EPO and erythropoiesis directly. Measurable levels of circulating cytokines may be found in stable dialysis patients, but, in the absence of inflammation, do not adversely affect the action of ESAs. In patients with impaired renal function and a normochromic, normocytic anemia, it is rare for the serum EPO level to be elevated. Therefore, measurement of EPO levels in such patients is not likely to guide clinical decision-making or ESA therapy. Anemia can develop relatively early in the course of CRF and has been associated with a serum creatinine as low as 2.0 mg/dL

A CKD staging system has been developed by the National Kidney Foundation through KDOQI and has classified CKD into five distinct stages, based on the level of kidney function using Glomerular Filtration Rate (GFR).

Stage 1 - Kidney damage with normal or increased GFR > 90

Stage 2 - Kidney damage with mild or decreased GFR 60-89

Stage 3 - Moderate decline in GFR 30-59

Stage 4 - Severe Decline in GFR 15-29

Stage 5 - Kidney failure <15 (for dialysis)

Anemia can occur in any of these stages but is more likely to be found in stages 3, 4 and 5

Specific coverage criteria:

End Stage Renal Disease (ESRD) when patients are ON dialysis (CMS Pub 100-2, Medicare Benefit Policy Manual, Chapter 11 "End Stage Renal Disease", §90) coverage is indicated when:

- The diagnosis is end stage renal disease; with

-Anemia of ESRD indicated by a hemoglobin of 10 gm/dl or less or a hematocrit of 30% or less at initiation of therapy.

-See the NCD in the coding guidelines for more complete information on coverage anemia in patients with ESRD.

Chronic kidney disease when patients are NOT on dialysis we cover ESAs when:

- The anemia with hgb/hct is 10 / 30% or less at initiation of therapy.

- The serum Creatinine is equal to or greater than 3, creatinine clearance less than 60 ml/min, or glomerular filtration rate (GFR) less than 60 mL/min/1.73 m²;

C. Coverage of EPO and DPA for Indications other than ESRD

EPO or darbepoetin may be a covered service for treatment of anemia when other treatable causes of anemia are identified and treated and one of the following clinical situations applies:

The patient must have, within the past 30 days, HCT 30 or below or HGB 10 or below, before coverage by WPS Medicare will begin. Where the patient has required a blood or red cell transfusion within the past month, you may use the most recent HCT or HGB before the transfusion.

1. For patients with anemia associated with cancer see NCD

2. Anemia related to therapy with Zidovudine (AZT) in acquired immunodeficiency syndrome (AIDS) or AIDS-related complex (ARC).

HIV infected patients taking AZT develop anemia. It has been observed that this anemia responds to exogenous erythropoietin therapy in the individuals who were receiving AZT doses of 4200 mg or less/week, and whose endogenous levels of erythropoietin are 500 MU/ml or less. Patients with AZT induced anemia whose endogenous serum erythropoietin levels are more than 500 MU/ml do not appear to respond to this therapy. It would be expected that the drug would be discontinued when there is lack of response following no more than 3 months of treatment or 3 months following the discontinuation of Zidovudine therapy.

3. Anemia associated with chemotherapeutic medications when medically necessary for a non-cancer diagnosis or following stem cell transplantation and associated immunosuppression.

*4. The patient carries a diagnosis of Myelodysplastic Syndrome (MDS)

Myelodysplastic syndromes are a heterogeneous group of hematological malignancies characterized by dysplastic (abnormal) and ineffective hematopoiesis (blood cell production) and a variable risk of transformation to acute leukemia.

Anemia is observed in 90 percent of individuals with MDS. Those MDS patients with an endogenous EPO level of less than 500 mU/mL are more likely to respond to erythropoiesis-stimulating agent ESA therapy. ESA therapy is indicated for patients with a confirmed diagnosis of MDS, when the anemia is symptomatic, there is a reasonable expectancy of longer survival and therapy is provided in order to end or reduce the need for transfusions.

When ESAs are used for the treatment of Myelodysplastic Syndrome, the following information must be included in the patient's record:

- Erythropoietin level (requires an EPO level less than or equal 500 IU/L).
- Report of bone marrow biopsy supporting diagnosis of myelodysplastic syndrome or chronic myelomonocytic leukemia as listed above.
- Indicate the start date at the beginning of the trial period.
- Indicate if treatment is responsive or non-responsive at the end of the trial. (A trial need not take the entire 12 weeks; if it is determined earlier that the patient is not responding, this must be documented in the patient's record.)
- The patient's medical record should contain laboratory results pertinent to treatment such as serum ferritin, serum transferrin, HGB or HCT: and
- A narrative evaluation regarding response to therapy

ESAs are covered for the treatment of anemia in MDS when the following criteria are met:

a. Patient with anemia associated with MDS with bone marrow blast count of less than 10 percent blasts (238.72, 238.73, 238.74, and 238.75)

b. Patient's anemia is symptomatic

c. Pretreatment Hgb level of <10 g/dL or Hct of <30 percent obtained within one week of the initial injection.

Dosing Management:

a. Dose, dosage frequency, and increases:

-If no increase in Hgb of 1 g/dL or greater in first month, increase dose to 60,000 units of EPO or proportionate increase in DPA dosage to 300 micrograms.

-If no increase in Hgb of 1 g/dL or greater in second month, increase dose to 80,000 units or a proportionate increase in DPA dosage to 400 micrograms.

-If no increase in Hgb of 1 g/dL or greater in third month, discontinue therapy.

b. Dosage should be titrated so that the Hgb is within a range of 10 - 12 g/dL or Hct of 30 - 36 percent.

c. Once the patient's Hgb is > 10 g/dL or Hct >30 percent, decrease the current dose by 10 - 25 percent to maintain the target range of 10-12 g/dL or 30-36 percent.

d. After 12 weeks of EPO/DPA therapy with the appropriate dose titrations, Hgb must increase by at least 1 g/dL or transfusion requirement must decrease by 50 percent resulting in a rate of two units per month or less for treatment to continue.

ESA therapy would not be covered if Hgb/Hct levels are above 12 g/dL/36 percent.

5. Anemia of Chronic disease (Anemia of Inflammatory disease) (285.29)

In anemia of chronic disease, inflammatory cytokines suppress the endogenous production of erythropoietin and erythropoiesis directly. This anemia usually results from a combination of slightly shortened red blood cell survival, the sequestration of iron in the reticuloendothelial systems, and epo levels that are less than expected for the degree of anemia. The diagnosis is usually exclusionary; meaning other causes of the anemia have been ruled out.

Common Features:

- low or normal serum iron

- low or normal iron-binding capacity levels

- elevated iron in reticulo-endothelial cell in bone marrow

Note: There may be variances in the above

To respond appropriately to exogenous erythropoietin administration, patients must have adequate available iron stores (i.e. normal or elevated ferritin levels and/or normal bone marrow iron stain). Further, their endogenous erythropoietin level must indicate poor responsiveness to the anemic process.

The severity of these anemias is usually moderate and they are rarely symptomatic or in need of therapy with EPO or DPA. The anemia usually resolves when the inflammatory process is successfully treated.

Anemia of cancer is not considered a chronic disease for this purpose and should not be billed as such.

Medicare will cover the use of EPO or DPA for the refractory anemia of chronic disease for patients with Rheumatoid Arthritis, Systemic Lupus Erythematosus, Chronic Hepatitis C, Regional Enteritis (or Crohn's Disease) and Ulcerative Colitis when all of the following (a, b, and c) conditions are met:

a. At least one of the conditions below:

- low or normal serum iron

- low or normal iron binding capacity

- normal or elevated serum ferritin

- adequate iron stores in bone marrow.

b. The pretreatment HCT level is 30 percent or less and/or if the patient has been transfusion dependent.

c. The pretreatment erythropoietin level is 100 MU/ml or less

Note: Lab results can be skewed if the patient has had transfusions or has been given iron supplements prior to determining the need for EPO or DPA. In instances such as this there must be written acknowledgement of this and the reasoning behind the need for these agents.

*Dosing Management:

a. Dose, dosage frequency, and increases:

-If no increase in Hgb of 1 g/dL or greater in first month, increase dose to 60,000 units of EPO or proportionate increase in DPA dosage to 300 micrograms.

-If no increase in Hgb of 1 g/dL or greater in second month, increase dose to 80,000 units or a proportionate increase in DPA dosage to 400 micrograms.

-If no increase in Hgb of 1 g/dL or greater in third month, discontinue therapy.

b. Dosage should be titrated so that the Hgb is within a range of 10 - 12 g/dL or Hct of 30 - 36 percent.

c. Once the patient's Hgb is > 10 g/dL or Hct >30 percent, decrease the current dose by 10 - 25 percent to maintain the target range of 10-12 g/dL or 30-36 percent.

d. After 12 weeks of EPO/DPA therapy with the appropriate dose titrations, Hgb must increase by at least 1 g/dL or transfusion requirement must decrease by 50 percent resulting in a rate of two units per month or less for treatment to continue.

6. Prophylactic pre-operative use (V07.8) for reduction of allogenic blood transfusions prior to elective hip and knee replacement surgery.

EPO or DPA is covered for use in patients:

- who are undergoing hip or knee surgery;
- have an anemia with a hemoglobin between 10 and 13 mg/dl. (this indication requires a lead time of at least 3 weeks prior to surgery);
- are not candidates for autologous blood transfusion;
- are expected to lose more than 2 units of blood; and
- have had a work-up so that their anemia appears to be that of chronic disease.

A weekly dosage regimen for 3 weeks prior to surgery (e.g., days 21, -14, -7) and on the day of surgery will be covered.

The components listed above must be documented in the medical record.

Patients receiving ESAs pre-operatively for reduction of allogeneic red blood cell transfusions: A higher incidence of deep venous thrombosis was documented in patients receiving ESAs who were not receiving prophylactic anticoagulation.

Coding Information

Bill Type Codes:

Contractors may specify Bill Types to help providers identify those Bill Types typically used to report this service. Absence of a Bill Type does not guarantee that the policy does not apply to that Bill Type. Complete absence of all Bill Types indicates that coverage is not influenced by Bill Type and the policy should be assumed to apply equally to all claims.

12x	Hospital-inpatient or home health visits (Part B only)
13x	Hospital-outpatient (HHA-A also) (under OPSS 13X must be used for ASC claims submitted for OPSS payment -- eff. 7/00)
22x	SNF-inpatient or home health visits (Part B only)
23x	SNF-outpatient (HHA-A also)
71x	Clinic-rural health
72x	Clinic-hospital based or independent renal dialysis facility
73x	Clinic-independent provider based FQHC (eff 10/91)
85x	Special facility or ASC surgery-rural primary care hospital (eff 10/94)

Revenue Codes:

Contractors may specify Revenue Codes to help providers identify those Revenue Codes typically used to report this service. In most instances Revenue Codes are purely advisory; unless specified in the policy services reported under other Revenue Codes are equally subject to this coverage determination. Complete absence of all Revenue Codes indicates that coverage is not influenced by Revenue Code and the policy should be assumed to apply equally to all Revenue Codes.

0634	Drugs requiring specific identification-EPO under 10,000 units
0635	Drugs requiring specific identification-EPO 10,000 units or more
0636	Drugs requiring specific identification-detailed coding (eff 3/92)

CPT/HCPCS Codes

EPO	
J0885	INJECTION, EPOETIN ALFA, (FOR NON-ESRD USE), 1000 UNITS
J0886	INJECTION, EPOETIN ALFA, 1000 UNITS (FOR ESRD ON DIALYSIS)
Darbepoetin alfa	
J0881	INJECTION, DARBEPOETIN ALFA, 1 MICROGRAM (NON-ESRD USE)
J0882	INJECTION, DARBEPOETIN ALFA, 1 MICROGRAM (FOR ESRD ON DIALYSIS)

ICD-9 Codes that Support Medical Necessity

Note: ICD-9 codes must be coded to the highest level of specificity.

EPO or DPA for ESRD on Dialysis J0886 or J0882
285.21 Anemia in end-stage renal disease

XX000 Not Applicable

2. EPO or DPA for indications other than ESRD on dialysis J0885 or J0881

*EPO or DPA for chronic renal disease not on dialysis J0885 or J0881
285.21 Anemia in end-stage renal disease
AND one of the following
585.3 - 585.9 Chronic renal disease (CRD) (Use one of these codes to indicate CRD not yet on dialysis).

XX000 Not Applicable

Use both the anemia code (285.8 or 285.9) and one of the following codes or combination of codes, according to the disease that is being treated:
042, 079.53 AZT treatment with AIDS

Use a third code to indicate the condition being treated Long term (current) use of other medications – High risk medications

Anemia associated with chemotherapeutic medications when medically necessary for a non-cancer diagnosis or following stem cell transplantation and associated immunosuppression. This would not be used to for neoplastic disease since that coverage is outlined in an NCD.

Drug induced anemia (this indicates the anemia is secondary to chemotherapy properly administered to treat a non-cancer diagnosis such as Hepatitis C treatment with ribavirin and interferon alfa or ribavirin peginterferon alfa.

238.72, 238.73, 238.74, 238.75 Myelodysplastic syndrome

- Chronic myelomonocytic leukemia (CMML)

V07.8 Prophylactic pre-operative use for reduction of allogenic blood transfusions prior to elective hip and knee replacement surgery.

XX000

Not Applicable

285.29 - Anemia of chronic disease and one of the following:

555.0-555.9 Crohn's disease

556.0-556.9 Ulcerative colitis

710.0 Systemic Lupus Erythematosus

714.0 Rheumatoid arthritis

714.1 Felty's syndrome

714.2 Other Rheumatoid arthritis with visceral or systemic involvement

XX000

Not Applicable

Diagnoses that Support Medical Necessity

ICD-9 Codes that DO NOT Support Medical Necessity

ICD-9 Codes that DO NOT Support Medical Necessity Asterisk Explanation

Diagnoses that DO NOT Support Medical Necessity

General Information

Documentation Requirements

Documentation supporting the medical necessity of this item, such as ICD-9 codes, must be submitted with each claim. Claims submitted without such evidence will be denied as being not medically necessary. Documentation supporting medical necessity may be requested. Medical record information should support the requirements of the policy. Example: laboratory reports and tests that support the diagnosis and required parameters listed in the policy.
See coding guidelines for electronic submission of documentation.

Appendices

Utilization Guidelines

1. Refer to the Indications and limitations of coverage for each condition to determine the information required in the medical record.
2. When ESAs are given for ESRD/CRD patients, the following information must be in the patients record and available upon request:
 - a. The current hematocrit or hemoglobin level and the date obtained.
 - b. Serum creatinine, with the date obtained. If a creatinine clearance was done, include that information, with the date obtained.
 - c. Patient's weight in kilograms.
 - d. Dose per kilogram.
3. For ESRD patients, the maximum number of administrations of epoetin alfa for a billing cycle is 13 times in 30 days and 14 times in 31 days (CMS Publication 100-04, Medicare Claims Processing Manual, Chapter 8, Section 60.4.1)

Darbepoetin alfa is given not more than once per week according to its Food and Drug Administration-approved labeling (see label issued March 24, 2006). For this reason, we will allow it to be billed a maximum of five times during any calendar month (CMS Publication 100-04, Medicare Claims Processing Manual, Chapter 8, Section 60.7.1)

Literature describes a significant increase in risk associated with hematocrit greater than 36. Prompt and judicious dose adjustments are anticipated in response to reaching the target hgb/hct (delayed reductions or reductions of less than 25% must be justified in the medical record.) The medical record must support the necessity of a target Hb/HCT greater than 12/36.

3. Medicare considers dosages exceeding 90,000 units per week for epoetin alfa or 200ug per week for darbepoetin alfa to be rarely reasonable and necessary. The medical justification for doses exceeding these amounts should be documented in the patient's record and made available for review upon request. This applies to all indications listed.

Sources of Information and Basis for Decision

WPS has consolidated the existing LCDs for MAC Jurisdiction 5 according to the instructions provided by CMS so that they are the same throughout the jurisdiction. In the vast majority of cases, one least restrictive LCD was selected as the jurisdictional LCD. In some cases, appropriate revisions, such as combining sections of LCDs that only addressed a portion of a general topic into a single, more complete document, were made to improve the clinical appropriateness of the LCD while keeping with the least restrictive requirement.

In situations where one or more of the states in the jurisdiction does not have an LCD on a topic, then the existing LCDs were reviewed and, based on the merits of the LCD, a decision was made to make the LCD jurisdictional or to have no LCD on that topic with the approval of CMS.

Some revisions of the existing LCDs were necessary to remove references to the former contractor and to update the Sources of Information and Basis for Decision. CPT, HCPCS and ICD-9 codes will be updated as necessary.

According to the J5 MAC contract, the J5 consolidated LCDs are posted on the web site for the 45 day final notification period prior to the policy implementation date. The MAC contractor is not required to utilize the formal notice and comment revision process specified in Chapter 13 of the Program Integrity Manual (PIM) until the consolidation process is final. However, WPS welcomes provider input regarding the J5 consolidated LCDs. Based on the comments received, LCDs will be revised as necessary during the transition from the existing to new contractor.

This policy does not reflect the sole opinion of the contractor or contractor medical director. Although the final decision rests with the contractor, this policy was developed in consideration of the active LCDs maintained by the preceding Medicare contractors for Jurisdiction 5.

Vardiman, James W. et al; The World Health Organization (WHO) classification of the Myeloid Neoplasms; Blood, Vol 100, Number 7, 10/01/2002

National Kidney Foundation Guidelines for the Treatment of Anemia of Chronic Renal Failure, 1997 (reiterated 2000)

Editorial: Erythropoietin For End Stage Renal Disease; NEJM; Vol. 339, NO 9; 08/27/98

Van Wyck, David B.; Iron Management During Recombinant Human Erythropoietin Therapy; Am J. of Kidney Diseases; Vol XIX, No.2 Supp1; 08/1989.

Wintrob's Clinical Hematology; 10th Edition, 1998, Vol. 2, P.2320

Pathology; 2nd Edition; Rubin, Emanuel; Farber, John, L.; J.B. Lippincott; 1998, pp1010-1029

Williams Hematology; 5th Edition, 1995, McCraw-Hill; Chapter 26

Heaney, Mark L., Golde, David, W.; Medical Progress: Myelodysplasia; NEJM; 05/27/99, Vol 340, No.21

Goldberg, Mark A., et.al.; A Safety and Efficacy Comparison Study of Two dosing regimens of Epoetin alfa in Patients Undergoing Major Orthopedic Surgery; The American Journal of Orthopedics; 08/96, pp 544-552.

Faris, P.M., et.al.; The Effects of Recombinant Human Erythropoietin on Perioperative Transfusion Requirements in Patients Having a Major Orthopaedic Operation; The Journal of Bone and Joint Surgery; Vol 78-A, NO 1; 01/96.

de Andrade. Robin J., et.al.; Baseline Hemoglobin as a Predictor of Risk of Transfusion and Response To Epoetin alfa in Orthopedic Surgery Patients; The American Journal of Orthopedics; 08/96, pp533-542.

Bierbaum, Benjamin E., et. al.; An Analysis of Blood Management in Patients Having a Total Hip or Knee Arthroplasty; The Journal of Bone and Joint Surgery; Vol 81-A, NO 1, 01/99, pp 2-10.

Canadian Orthopedic Perioperative Erythropoietin Study Group; Effectiveness of Perioperative Recombinant Human Erythropoietin in Elective Hip Replacement; The Lancet; Vol 341, NO 8855; 05/15/93.

Goodnough, Lawrence, T., et. al., Medical Progress: Transfusion Medicine (First of Two Parts) B; Blood Transfusion; NEJM; Vol 340, NO 6; 02/11/99.

Goodnough, Lawrence, T., et. al., Medical Progress: Transfusion Medicine (Second of Two Parts) B Blood Conservation; NEJM; Vol 340, NO 7, 02/18/99.

Pincus, Theodore, et.al.; Multicenter Study of Recombinant Human Erythropoietin in Correction of Anemia in Rheumatoid Arthritis; AmJM; Vol 89; 08/1990.

Krantz, Sanford, B., Pathogenesis and Treatment of the Anemia of Chronic Disease; AJMS, Vol. 307, No.5; 05/1994

Southgate, W. Michael; Anemia of Prematurity; eMedicine Journal, Vol3, No1. 01/23/2002

Smith RE Jr, Jaiyesimi IA, Meza LA, et. al: Novel Erythropoiesis Stimulating Protein (NESP) For The Treatment Of Anaemia Of Chronic Disease Associated With Cancer. Br J Cancer. 2001 Apr;84 Suppl 1:24-30.
Smith, R. E., Jr., N. S. Tchekmedyian, et al. (2003). "A dose and schedule-finding study of darbepoetin alpha for the treatment of chronic anaemia of cancer." Br J Cancer 88(12): 1851-8.

United States Pharmacopoeia (USP), Volume 1; Drug Information for the Health Care Professional, 23rd edition, 2003.

2007 Additions

Amgen, Inc., Dear Healthcare Professional Letter for Aranesp® [darbepoetin alfa], US Food and Drug Administration, Rockville, MD; Accessed on 1/26/2007. Available at:
http://www.fda.gov/medwatch/safety/2007/Aranesp_DHCP_012707.htm

Besarab, A., et al; The effects of Normal as Compared with Low Hematocrit Values In Patients with Cardiac Disease Who are Receiving Hemodialysi and Epoetin; NEJM Vol. 339,: 584 -590; August 27, 1998

Bohlius, J., et al; Recombinant Human Erythroprotiens and Cancer Patients : Updated Meta-Anaysis of 57 Studies Including 9353 Patients; Jour. Of the Am. Cancer Institute, Vol. 98, No. 10, May 17, 2006, 708-714

Cotter, Dennis et.al.; Translating Epoetin Research Into Practice: The Role Of Government And The Use Of Scientific Evidence; Health Affairs; Vol. 25, No. 5; Sept./OCT, 2006

Drueke, Tilman B, et al; Normalization of Hemoglobin level in Patients with Chronic Kidney Disease and Anemia; NEJM; 355, 20; Nov 16, 2006; 2071-2084

EDITORIALS; Preaching and Practice: Evidence-Based Medicine and the Accountability of Nephrologists Within the Health Care System. The Implications of the Findings oft he Cost-Saving Potential of Subcutaneous Versus Intravenous Epoetin Therapy; American Journal of Kidney Diseases, Vol 40, No 3 (September), 2002: pp 662-663

FDA News, March 9, 2007

Henke, M., et al; Erythropoietin to Treat Head and Neck Cancer Patients with Anaemia Undergoing Radiotherapy: Randomized, Double-blind, Placebo- controlled Trial; The Lancet Vol. 362; OCT. 18, 2003
*FDA Drug Safety Erythropoiesis-Stimulating Agents (ESAs) - FDA and Amgen, the manufacturer of the three ESA-agents, have changed the full prescribing information for these drugs. The new product labeling includes a new boxed warning, updated warning, and change to the dosage and administration sections for all ESAs.; 11/08/2007

Lai , Stephen Y. and Grandis, Jennifer R.; EDITORIAL : Understanding the Presence and Function of Erythropoietin Receptors on Cancer Cells; Journal of Clinical Oncology, Vol. 24, No 29 October 10, 2006: pp. 4675-4676

Leyland-Jones, B., et al; Maintaining Normal Hemoglobin Levels with Epoetin Alpha in Mainly Nonanemic Patients with Metastatic Breast Cancer Receiving First-Line Chemotherapy: A Survival Study; Journal of Clinical Oncology; Vol. 23, No. 25; September 1, 2005; 5960-5972

Ludwig, H; Epoetin in Cancer Related Anaemia; Nephrology Dialysis Transplantation; 1999, 14 (Supp 2): 85-92

Ma, Jennie Z, et al; Hematocrit Level and Associated Mortality in Hemodialysis Patients; J Am Soc Nephrol 10: 610–619, 1999

National Comprehensive Cancer Network; Clinical Practice Guidelines in Oncology - v.2.2006. Cancer- and Treatment-Related Anemia

Quirt, BY, I. et al; Epoetin Alpha Therapy Increases Hemoglobin Levels and Improves Quality of Life in Patients With Cancer-Related Anemia Who Are Not Receiving Chemotherapy and Patients With Anemia Who Are Receiving Chemotherapy; Journal of Clinical Oncology, Vol. 19, No. 21 Nov., 2001: 4126-4134

Rizzo, JD, Lichtin AE, Woolf SH, et al. Use of epoetin in patients with cancer: evidence-based clinical practice guidelines of the American Society of Clinical Oncology and the American Society of Hematology. J Clin Oncol. October 2002;20(19) 4083-4107.

*Rizzo, JD, Sommerfeld MR, Hagerty KL, Seidenfeld J, Bohlius J, BennetCL, Cella DF, Djulbegovic B, Goode MJ, Jakubowski, Rarick, Regan DH, Lichtin AE; American Society of Hematology/American Society of Clinical Oncology 2007 clinical practice guideline update on the use of epoetin and darbepoetin; Blood (online) 10/23/2007

Results from a phase 3, randomized, double-blind, placebo-controlled study of darbepoetin alfa for the treatment of anemia in patients with active cancer not receiving chemotherapy or radiotherapy Un-published

Singh, Ajay K., et al; Correction of Anemia with Epoetin Alpha in Chronic Kidney Disease; NEJM, 2006;355:2085-98.

Singh, Zeba N. et al; Therapy-Related Myelodysplastic Syndrome: Morphologic Sub-classification May Not Be Clinically Relevant; Am J Clin Pathol. 2007; 127 (2):197-205. ©2007 American Society for Clinical Pathology; Posted 02/22/2007

Wright, James R. et al; Randomized, Double-Blind, Placebo-Controlled Trial of Erythropoietin in Non–Small-Cell Lung Cancer With Disease-Related Anemia; Journal of Clinical Oncology, Vol. 25, No 9 (March 20), 2007: pp. 1027-1032

United States Pharmacopoeia (USP) Revision 02/2007

Other Carrier policies including: NGA, Cigna, First Coast, Trailblazer and Noridian

Advisory Committee Meeting Notes

Start Date of Comment Period**End Date of Comment Period****Start Date of Notice Period**

10/01/2009

Revision History Number

3

Revision History Explanation

*10/01/2009 ICD-9 code 285.21-Anemia in end-stage renal disease combined with one of the following ICD-9 codes 585.3 - 585.9- Chronic renal disease (CRD) with CPT codes J0885 or J0881

07/30/2009: Restored accidental removal of contract number 05392 (WPS Part B MAC Eastern Missouri), effective 03/01/08. Correctly removed contract number 05392 effective 8/1/2009, as it is being combined with contractor number 05302 (WPS Part B MAC Missouri - Entire State.)

06/30/2009 The contractor number 05392 will no longer be valid as of 8/1/2009 as it will be joining with the W MO number.

added Missouri Eastern

Reason for Change**Last Reviewed On Date**

10/01/2009

Related Documents

This LCD has no Related Documents.

LCD Attachments

[Billing and Coding Guidelines](#) (PDF - 57,005 bytes)

All Versions

Updated on 09/25/2009 with effective dates 11/16/2009 - N/A

Updated on 07/30/2009 with effective dates 08/01/2009 - 11/15/2009

Updated on 07/30/2009 with effective dates 03/01/2008 - 07/31/2009

Updated on 07/17/2009 with effective dates 03/01/2008 - N/A

Updated on 05/23/2008 with effective dates 03/01/2008 - N/A

Updated on 05/15/2008 with effective dates 03/01/2008 - N/A

Updated on 04/25/2008 with effective dates 03/01/2008 - N/A