Darbepoetin (Aranesp®) **Policy Number: M-0009**
Revision: 1 **Last Update: 3/19/2013**

Payment will not be made for any use of these drugs outside of the criteria without prior authorization. The member may not be billed unless the member explicitly agrees in writing to be responsible for the charges in accordance with the contract/provider manual. Prior authorization will only be given if the provider demonstrates the intended use meets Medicare coverage guidelines.

Coverage Guidelines:

End Stage Renal Disease (ESRD)

Erythropoietin Analogues (EA) are covered for the treatment of anemia for patients with chronic renal failure (ESRD) in the following clinical settings:

1. When EA are administered in the renal dialysis facility:
    A. When EA are administered in a renal dialysis facility, coverage is available through Part A whether the facility is independent or hospital-based. "Incident to" provisions do not apply in these settings.

    B. When EA are administered in a physician's office, (administered "incident to" a physician's service), they are considered a Medicare Part B service.
2. When EA are administered during an unscheduled or emergency dialysis treatment in the outpatient hospital setting.

3. When EA are self-administered in the home by any dialysis patient (or patient care giver) who is determined competent to use the drug and meets the following conditions:
    A. Plan of Care - must have a current care plan for monitoring home use of EA which includes the following:
        i. Review of the diet and fluid intake for aberrations as indicated by hyperkalemia and elevated blood pressure secondary to volume overload;

ii. Review of medications to ensure adequate provisions of supplemental iron;

iii. Ongoing evaluations of hematocrit and iron stores;

iv. Reevaluation of dialysis prescription taking into account the patient's increased appetite and red blood cell volume;

v. Method of physician and facility follow-up on blood tests and mechanism (such as a patient log) for keeping the physician informed of the results;

vi. Training of the patient to identify the signs and symptoms of hypotension and hypertension; and

vii. The decrease or discontinuance of EA if hypertension is uncontrollable.

B. Patient selection - The dialysis facility or physician responsible for all dialysis related services furnished to the patient must make a comprehensive assessment that includes the following:

i. Pre-selection monitoring of patient's hematocrit (or hemoglobin), serum iron, transferrin saturation, serum ferritin and blood pressure.

ii. The patient must be a dialysis patient

iii. Has a hematocrit as follows:

a. For a patient who is initiating EA treatment no higher than 30 percent unless there is medical documentation showing the need for EA despite hematocrit higher than 30 percent. Patients with severe angina, severe pulmonary distress, or severe hypotension may require EA to prevent adverse symptoms even if they have higher hematocrit levels.

b. For a patient who has been receiving EA from the facility or the physician, between 30 and 36 percent.

iv. Is under the care of a physician who is responsible for all dialysis-related services and who prescribes EA and follows the drug labeling instructions when monitoring the EA home therapy; and a renal dialysis facility that establishes the plan of care and monitors the progress of the home EA therapy.

v. The assessment must find that the patient or caregiver is able to inject the EA using aseptic techniques and is capable of reading and understanding the drug labeling.

vi. The assessment must also find that EA can be stored in the patient's residence under refrigeration and the patient is aware of the potential hazard of a child's having access to the drug and syringes.

C. The Physician or Dialysis Facility must:

i. Develop a protocol that follows the drug label instructions

ii. Make the protocol available to the patient to ensure safe and effective home use of EA;

iii. Through the amounts prescribed, ensure that the drug on hand at any time does not exceed a 2-month supply, and

iv. Maintain adequate records to allow quality assurance for review.

Chronic Kidney Disease (CKD) not on Dialysis

EA are considered medically necessary for CKD patients not on dialysis if the requirements in

the *Limitations* section are documented.

Secondary Anemia (Non-CKD)

EA are covered for the treatment of symptomatic anemia that is secondary to:

1. Effects of cancer related chemotherapy. This is considered an "adverse effect" and is covered using the appropriate E ICD-9 code along with the anemia ICD-9 code.

2. HIV and Hepatitis C by drug therapies such as zidovudine (AZT) and ribavirin.

3. Myelodysplastic syndrome (MDS). An erythropoietin serum level of <500 mU/ml is necessary for treatment in all patients with anemia attributable to myelodysplastic syndrome. For clarification, terminology that may be used on the bone marrow biopsy report to define myelodysplastic conditions are as follows:

    A. Myelodysplastic disease, disorder, or syndrome
    B. Myelodysplasia
    C. Refractory anemia
    D. Refractory anemia with ringed sideroblasts; Sideroblastic anemia
    E. Increased stainable iron stores with ringed sideroblasts
    F. Refractory anemia with excess blasts
    G. Refractory anemia with excess blasts in transition (to acute leukemia)
    H. Pre-leukemia, pre-leukemic syndrome
    I. Chronic myelodysplastic leukemia
    J. Dysmyelopoietic syndrome
    K. Refractory dysmyelopoietic anemia

4. Inflammatory diseases, to include: Rheumatoid arthritis, Ulcerative colitis, Regional enteritis, and Systemic lupus erythematosus.

Pre-operative Use

EA are covered preoperatively for anemic patients scheduled to undergo elective, noncardiac, nonvascular surgery and who:

1. Have an anemia with a hematocrit between 30 - 39 percent; and
2. Are not a candidate for autologous blood transfusion; and
3. Are expected to lose more than 2 units of blood; and
4. Have had a workup so that their anemia appears to be that of chronic disease.

Coding Information:

HCPCS Code(s)

J0881	INJECTION, DARBEPOETIN ALFA, 1 MICROGRAM (NON-ESRD USE)
J0882	INJECTION, DARBEPOETIN ALFA, 1 MICROGRAM (FOR ESRD ON DIALYSIS)

For HCPCS Code J0882

Both codes below are required

ICD-9 Code(s)

285.21	ANEMIA IN CHRONIC KIDNEY DISEASE
585.6	END STAGE RENAL DISEASE

For HCPCS Code J0881

Each claim must contain an ICD-9 code from the following anemia list plus an ICD-9 code from the appropriate indication

Anemia

284.89	OTHER SPECIFIED APLASTIC ANEMIAS
285.0	SIDEROBLASTIC ANEMIA
285.21	ANEMIA IN CHRONIC KIDNEY DISEASE
285.22	ANEMIA IN NEOPLASTIC DISEASE
285.29	ANEMIA OF OTHER CHRONIC DISEASE
285.3	ANTINEOPLASTIC CHEMOTHERAPY INDUCED ANEMIA

285.9	ANEMIA UNSPECIFIED

Indication

042	HUMAN IMMUNODEFICIENCY VIRUS (HIV) DISEASE
070.41	ACUTE HEPATITIS C WITH HEPATIC COMA
070.44	CHRONIC HEPATITIS C WITH HEPATIC COMA
070.51	ACUTE HEPATITIS C WITHOUT MENTION OF HEPATIC COMA
070.54	CHRONIC HEPATITIS C WITHOUT HEPATIC COMA
070.71	UNSPECIFIED VIRAL HEPATITIS C WITH HEPATIC COMA
208.10	CHRONIC LEUKEMIA OF UNSPECIFIED CELL TYPE, WITHOUT MENTION OF HAVING ACHIEVED REMISSION
238.7-238.75	ESSENTIAL THROMBOCYTHEMIA - MYELODYSPLASTIC SYNDROME, UNSPECIFIED
403.11	HYPERTENSIVE CHRONIC KIDNEY DISEASE, BENIGN, WITH CHRONIC KIDNEY DISEASE STAGE V OR END STAGE RENAL DISEASE
403.91	HYPERTENSIVE CHRONIC KIDNEY DISEASE, UNSPECIFIED, WITH CHRONIC KIDNEY DISEASE STAGE V OR END STAGE RENAL DISEASE
404.13	HYPERTENSIVE HEART AND CHRONIC KIDNEY DISEASE, BENIGN, WITH HEART FAILURE AND CHRONIC KIDNEY DISEASE STAGE V OR END STAGE RENAL DISEASE
404.91	HYPERTENSIVE HEART AND CHRONIC KIDNEY DISEASE, UNSPECIFIED, WITH HEART FAILURE AND WITH CHRONIC KIDNEY DISEASE STAGE I THROUGH STAGE IV, OR UNSPECIFIED
404.93	HYPERTENSIVE HEART AND CHRONIC KIDNEY DISEASE, UNSPECIFIED, WITH HEART FAILURE AND CHRONIC KIDNEY DISEASE STAGE V OR END STAGE RENAL DISEASE
555.0-555.9	REGIONAL ENTERITIS OF SMALL INTESTINE - REGIONAL ENTERITIS OF UNSPECIFIED SITE
556.0-556.9	ULCERATIVE (CHRONIC) ENTEROCOLITIS - ULCERATIVE COLITIS UNSPECIFIED
585.3	CHRONIC KIDNEY DISEASE, STAGE III (MODERATE)
585.4	CHRONIC KIDNEY DISEASE, STAGE IV (SEVERE)
585.5	CHRONIC KIDNEY DISEASE, STAGE V
710.0	SYSTEMIC LUPUS ERYTHEMATOSUS
714.0-714.4	RHEUMATOID ARTHRITIS - CHRONIC POSTRHEUMATIC ARTHROPATHY

E930.7	ANTINEOPLASTIC ANTIBIOTICS CAUSING ADVERSE EFFECTS IN THERAPEUTIC USE
E931.7	ANTIVIRAL DRUGS CAUSING ADVERSE EFFECTS IN THERAPEUTIC USE
E933.1	ANTINEOPLASTIC AND IMMUNOSUPPRESSIVE DRUGS CAUSING ADVERSE EFFECTS IN THERAPEUTIC USE
V02.62	CARRIER OR SUSPECTED CARRIER OF HEPATITIS C
V07.8	OTHER SPECIFIED PROPHYLACTIC OR TREATMENT MEASURE
V08	ASYMPTOMATIC HUMAN IMMUNODEFICIENCY VIRUS (HIV) INFECTION STATUS

Limitations:

End Stage Renal Disease (ESRD)

EA are not reasonable and necessary for patients with hematocrits greater than 36%.

Chronic Kidney Disease - Not on Dialysis

1. EA should be limited to individuals having:
    A. Pre-treatment HCT less than 33%
    B. Non-correctable anemia
    C. Related significant reduction in activities of daily living (ADLs) and one or more of the following symptoms:
        i. Weakness
        ii. Dyspnea
        iii. Dizziness
        iv. Marked Fatigue
        v. Chest Pain
        vi. Postural Hypotension
2. EA are not reasonable and necessary for patients with hematocrits greater than 36%.
3. An evaluation for other causes of anemia (e.g. iron deficiency, folic acid deficiency, vitamin deficiency) should be addressed and treated where correctable.

Secondary Anemia (Non-CKD)

1. Effective May 1, 2007, EA will not be covered in the treatment of anemia secondary to cancer.

2. EA for treatment of Myeloid Malignancies is not covered. The following diagnoses are considered to be classified as myeloid malignancies and therefore are non-covered with or without chemotherapy:
    A. Myeloid leukemia;
    B. Monocytic leukemia;
    C. Other specified and unspecified leukemias;
    D. Personal history of myeloid leukemia. (May occasionally be approved with documentation if the myeloid leukemia is in complete remission AND the indication for epoetin is unrelated to either the myeloid leukemia or its treatment.)
3. EA, in the treatment of anemia secondary to chemotherapy is limited to a hemoglobin level of < 10% (or HCT <30%) prior to initiation of therapy **and for maintenance of therapy**.

4. EA, in the treatment of anemia secondary to chemotherapy, will not be covered beyond **8 weeks** from the last chemotherapy administration.

5. EA, in the treatment of anemia in MDS, HIV, Rheumatoid arthritis, Ulcerative colitis, Regional enteritis, Systemic lupus erythematosus, and Hepatitis C drug therapies should be limited to individuals having:

    A. Pre-treatment HCT less than 33%
    B. Non-correctable anemia
    C. Related significant reduction in activities of daily living (ADLs) and one or more of the following symptoms:
        i. Weakness
        ii. Dyspnea
        iii. Dizziness
        iv. Marked Fatigue
        v. Chest Pain
        vi. Postural Hypotension

Background:

Erythropoietin (EPO) is a hormone produced by the kidney that promotes the formation of red blood cells in the bone marrow. EPO is a glycoprotein (a protein with a sugar attached to it). EPO is the prime regulator of red blood cell production. Its major functions are to promote the differentiation and development of red blood cells and to initiate the production of

hemoglobin, the molecule within red cells that transports oxygen. Aranesp stimulates erythropoiesis by the same mechanism as endogenous erythropoietin.

Black Box Warning:

WARNING: ESAs INCREASE THE RISK OF DEATH, MYOCARDIAL INFARCTION, STROKE, VENOUS THROMBOEMBOLISM, THROMBOSIS OF VASCULAR ACCESS AND TUMOR PROGRESSION OR RECURRENCE

Chronic Kidney Disease:

- **In controlled trials, patients experienced greater risks for death, serious adverse cardiovascular reactions, and stroke when administered erythropoiesis-stimulating agents (ESAs) to target a hemoglobin level of greater than 11 g/dL.**
- **No trial has identified a hemoglobin target level, Aranesp dose, or dosing strategy that does not increase these risks.**
- **Use the lowest Aranesp dose sufficient to reduce the need for red blood cell (RBC) transfusions**

Cancer:

- **ESAs shortened overall survival and/or increased the risk of tumor progression or recurrence in clinical studies of patients with breast, non-small cell lung, head and neck, lymphoid, and cervical cancers.**
- **Because of these risks, prescribers and hospitals must enroll in and comply with the ESA APPRISE Oncology Program to prescribe and/or dispense Aranesp to patients with cancer. To enroll in the ESA APPRISE Oncology Program, visit www.esa-apprise.com or call 1-866-284-8089 for further assistance**
- **To decrease these risks, as well as the risk of serious cardiovascular and thromboembolic reactions, use the lowest dose needed to avoid RBC transfusions.**
- **Use ESAs only for anemia from myelosuppressive chemotherapy.**
- **ESAs are not indicated for patients receiving myelosuppressive chemotherapy when the anticipated outcome is cure.**
- **Discontinue following the completion of a chemotherapy course.**

Definitions:

EA—Erythropoietin Analogues. Medications that are used to stimulate red blood cell (RBC) production in the bone marrow, thereby correcting anemia, minimizing the need for transfusion requirements, and improving the quality of life for patients.

EPO—Erythropoietin. A hormone produced by the kidney that promotes the formation of red blood cells in the bone marrow.

ESRD—End Stage Renal Disease

HCPCS Code—Healthcare Common Procedure Coding System - A system of letter and number codes assigned to procedures, medications, supplies and equipment used for pricing and billing.

ICD-9 Code—International Classification of Disease, 9th edition. A standardized classification of disease, injuries, and causes of death, by etiology and anatomic localization and codified into a 6-digit number, which allows clinicians, statisticians, politicians, health planners and others to speak a common language, both US and internationally.

References:

1. Aranesp [package insert]. Thousand Oaks, CA: Amgen, Inc.; 2011. Available at: http://pi.amgen.com/united_states/aranesp/ckd/aranesp_pi_hcp_english.pdf. Accessed May 23, 2012.
2. Local Coverage Article for Drugs and Biologicals: Erythropoetin Analogues (L30024) (Revision 6). Available at: http://www.cms.gov/medicare-coverage-database/details/lcd-details.aspx?LCDId=30024&ContrId=213&ver=28&ContrVer=1&CoverageSelection=Both&ArticleType=All&PolicyType=Final&s=Alabama&CptHcpcsCode=J0885&clickon=search&bc=gAAAABAAAAAA&. Accessed May 23, 2012.
3. Micromedex® 2.0-Aranesp. Available at: http://www.thomsonhc.com/micromedex2/librarian/ND_T/evidencexpert/ND_PR/evidencexpert/CS/12CBCB/ND_AppProduct/evidencexpert/DUPLICATIONSHIELDSYNC/17C3A7/ND_PG/evidencexpert/ND_B/evidencexpert/ND_P/evidencexpert/PFActionId/evidencexpert.DisplayDrugpointDocument?docId=926699&contentSetId=100&title=Darbepoetin+Alfa&servicesTitle=Darbepoetin+Alfa&topicId=dosingAndIndicationsSection&subtopicId=nonfdaSection. Accessed May 23, 2012.

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For the Archived Policy, please go to http://www.vivaprovider.com/Resources/CoveragePolicies.aspx and click on the Archived Policies Link.