09-J4000-90

Original Effective Date: 08/15/24

Reviewed: 07/10/24

Revised: 01/01/25

Subject: Vadadustat (Vafseo)

THIS MEDICAL COVERAGE GUIDELINE IS NOT AN AUTHORIZATION, CERTIFICATION, EXPLANATION OF BENEFITS, OR A GUARANTEE OF PAYMENT, NOR DOES IT SUBSTITUTE FOR OR CONSTITUTE MEDICAL ADVICE. ALL MEDICAL DECISIONS ARE SOLELY THE RESPONSIBILITY OF THE PATIENT AND PHYSICIAN. BENEFITS ARE DETERMINED BY THE GROUP CONTRACT, MEMBER BENEFIT BOOKLET, AND/OR INDIVIDUAL SUBSCRIBER CERTIFICATE IN EFFECT AT THE TIME SERVICES WERE RENDERED. THIS MEDICAL COVERAGE GUIDELINE APPLIES TO ALL LINES OF BUSINESS UNLESS OTHERWISE NOTED IN THE PROGRAM EXCEPTIONS SECTION.

DESCRIPTION:

Anemia is a common complication of chronic kidney disease (CKD) due to the inability of the kidney to produce erythropoietin. This decreases the production of red blood cells and onset of symptoms associated with chronic anemia.

Vadadustat (Vafseo) and daprodustat (Jesduvroq) are FDA-approved for the treatment of anemia due to dialysis dependent (DD-CKD). They work by inhibiting hypoxia-inducible factor prolyl hydroxylase (HIF-PH) to stimulate endogenous erythropoietin production. Erythropoietin stimulating agents (epoetin alfa, darbepoetin alfa, methoxy polyethylene glycol-epoetin beta) are also FDA-approved for the treatment of patients with anemia due to DD-CKD.

Vadadustat was evaluated in subjects with anemia due to DD-CKD who were being treated with an ESA in two randomized, active-controlled, event-driven trials. Participants were on dialysis for at least 16 weeks in one trial and 12 weeks in another trial prior to randomization. Participants were excluded if anemia was considered to be due to causes other than CKD or if they had uncontrolled hypertension or a recent cardiovascular event. Medications were dosed to maintain a hemoglobin target between 10 to 11 g/dL in the US and 10 to 12 g/dL outside of the US. The main primary outcomes were the mean change in the hemoglobin level from baseline to Weeks 24 through 36 and the first occurrence of a major adverse cardiovascular event (MACE; defined as all-cause mortality, nonfatal MI, and nonfatal stroke). Vadadustat was shown to be noninferior to darbepoetin in the mean change in Hgb from baseline to week 24 through 36 (adjusted least squares mean change in trial 1, 1.3 g/dL versus 1.6 g/dL and trial 2, 0.2 g/dL versus 0.4 g/dL). The hazard ratio for the time to first occurrence of MACE also met non-inferiority(0.96, 95% CI, 0.83, 1.11). The most frequently occurring adverse reactions were hypertension and diarrhea.

Vadadustat contains a black box warning of the risk of arterial and venous thrombotic events that may be fatal, including myocardial infarction, stroke, venous thromboembolism and vascular access thrombosis. Patients with a history of myocardial infarction, cerebrovascular event or acute coronary syndrome within the 3 months prior to starting therapy should avoid use.

POSITION STATEMENT:

Initiation of vadadustat [Vafseo] meets the definition of **medical necessity** when **ALL** of the following are met:

1. Anemia due to chronic kidney disease
    a. Member has been receiving dialysis for at least three months
    b. Within the last 4 weeks, evaluation of the member's iron status includes **BOTH** of the following (unless member is receiving concurrent intravenous iron):
        i. Transferrin saturation is 20% or more
        ii. Ferritin is 100 ng/mL or more
    c. Within the last 4 weeks, member's hemoglobin is less than 11 g/dL or hematocrit is less than 33% - lab documentation must be submitted
    d. Other causes of anemia (e.g., hemolysis, bleeding) have been ruled out
    e. Member had an inadequate response, contraindication, or intolerance to **ONE** of the following – documentation must be submitted:
        i. epoetin alfa [Procrit, Epogen]
        ii. epoetin alfa-epbx [Retacrit]
        iii. darbepoetin [Aranesp]
        iv. methoxy polyethylene glycol-epoetin beta (Mircera)
    f. Member does not have uncontrolled hypertension
    g. Use is not combined with an erythropoietin stimulating agent (ESA)* or daprodustat (Jesduvroq)
    h. Dose does not exceed 600 mg daily

Approval duration: 6 months

Continuation of vadadustat [Vafseo] meets the definition of **medical necessity** when **ALL** of the following criteria are met:

1. The member has a beneficial clinical response to therapy (defined as a rise in hemoglobin from pre-treatment baseline within 24 weeks of therapy initiation for anemia of chronic kidney disease) and **EITHER** of the following:
    a. Member has been approved by Florida Blue or another healthplan in the past 6 months
    b. Member has previously met Florida Blue's initial criteria for coverage in the past 6 months

2. Within the past 3 months, evaluation of the member's iron status includes **BOTH** of the following(unless member is receiving concurrent intravenous iron):
    a. Transferrin saturation is 20% or more
    b. Ferritin is 100 ng/mL or more
3. The member's hemoglobin is less than 11 g/dL or hematocrit is less than 33%
4. Member does not have uncontrolled hypertension
5. Use is not combined with an erythropoietin stimulating agent(ESA)* or daprodustat (Jesduvroq)
6. Dose does not exceed 600 mg daily

*Note: ESA may be used temporarily as rescue therapy or prior to transitioning to vadadustat

Approval duration: 6 months

DOSAGE/ADMINISTRATION:

For the treatment of anemia due to chronic kidney disease (CKD) in adults who have been receiving dialysis for at least 3 months.

Individualize dosing and use the lowest dose sufficient to reduce the need for red blood cell transfusions. Do not target a hemoglobin level higher than 11 g/dL.

For adults not treated with an ESA, the starting dose is 300 mg orally once a day.

For adults being switched from an ESA, the starting dose is 300 mg orally once daily.

Following initiation of therapy and after each dose adjustment, monitor hemoglobin every 2 weeks for the first month and then every 4 weeks thereafter. If the dose needs to be adjusted, increase no more frequently than every 4 weeks in increments of 150 mg to maintain hemoglobin within 10 g/L to 11 g/L. The dose ranges from 150 mg to a maximum of 600 mg per day. Decrease the dose or interrupt if hemoglobin increases rapidly (greater than 1 g/dL over 2 weeks or greater than 2 g/dL over 4 weeks) or if the hemoglobin exceeds 11 g/dL. The dose can be resumed at 150 mg less than prior to interruption.

Do not continue treatment beyond 24 weeks of therapy if a clinically meaningful increase in hemoglobin level is not achieved.

PRECAUTIONS:

Boxed warning: increased risk of death, myocardial infarction, stroke, venous thromboembolism, and thrombosis of vascular access. Targeting a hemoglobin level greater than 11 g/dL is expected to further increase the risk of death and arterial venous thrombotic events, as occurs with erythropoietin stimulating agents, which also increase erythropoietin levels. No trial has identified a hemoglobin target

level, or dose that does not increase these risks. Use the lowest dose to reduce the need for red blood cell transfusions.

Warnings/precautions:

Risk of hospitalization for heart failure: increased in patients with history of heart failure.

Hepatotoxicity: Measure ALT, AST, and bilirubin prior to initiation, monthly after initiation for the first 6 months, then as clinically indicated. Discontinue if ALT or AST is persistently elevated or accompanied by elevated bilirubin.

Hypertension: Worsening hypertension, including hypertensive crisis may occur. Monitor blood pressure. Adjust anti-hypertensive therapy as needed.

Seizures: Seizures have occurred in patients with CKD. Monitor for new-onset seizures, premonitory symptoms, or change in seizure frequency.

Gastrointestinal erosion: Gastric or esophageal erosions and gastrointestinal bleeding have been reported.

Not indicated for treatment of anemia of CKD in patients who are not dialysis-dependent.

Malignancy: May have unfavorable effects on cancer growth. Not recommended if active malignancy.

BILLING/CODING INFORMATION:

HCPCS Coding

J0901	Vadadustat, oral, 1 mg (for ESRD on dialysis)

ICD-10 Diagnosis Codes That Support Medical Necessity

D63.1	Anemia in chronic kidney disease

REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT**.

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Part D: Florida Blue has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline.

Medicare Advantage: No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of the last guideline review date.

DEFINITIONS:

Erythropoietin: a protein naturally made in the kidneys, which acts on the bone marrow to stimulate the body's production of red blood cells.

ESRD: end-stage renal disease (kidney failure).

Hematocrit: a method for determining the volume of packed red blood cells in a blood specimen.

Hemoglobin: a method for measuring the oxygen carrying capacity of the red blood cells.

RELATED GUIDELINES:

Erythropoiesis Stimulating Agents, 09-J0000-31

Daprodustat (Jesduvroq), 09-J4000-89

OTHER:

None

REFERENCES:

1. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2024. URL www.clinicalpharmacilogy-ip.com Accessed 06/27/24.
2. Micromedex® Healthcare Series [Internet Database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed 06/27/24.
3. Vadadustat (Vafseo) [package insert] Akebia Therapeutics, Inc. Cambridge (MA): March 2024.

COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 07/10/24.

GUIDELINE UPDATE INFORMATION:

08/15/24	New Medical Coverage Guideline
01/01/25	Revision: Added HCPCS code J0901 and deleted code J3490.