09-J4000-89

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Reviewed: 07/10/24

Revised: 00/00/00

Subject: Daprodustat (Jesduvroq)

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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.

Daprodustat (Jesduvroq) and vadadustat (Vafseo) 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 (ESA, epoetin alfa, darbepoetin alfa, methoxy polyethylene glycol-epoetin beta) are also FDA-approved for the treatment of patients with anemia due to DD-CKD.

Daprodustat was evaluated in subjects with anemia due to DD-CKD who were being treated with an ESA in a randomized, active-controlled, event-driven trial. Prior ESAs were continued during the screening and run-in periods. Patients were on dialysis for at least 4 months prior to treatment and were randomized to daprodustat or recombinant human erythropoietin (rhEPO) control (IV epoetin alfa for hemodialysis [HD] patients and subcutaneous [SC] darbepoetin alfa for peritoneal dialysis [PD] patients). Patients were excluded if the ferritin was less than or equal to 100 mcg/L or transferrin saturation was less than or equal to 20%. Patients were also excluded if there were other causes of anemia, cardiovascular abnormalities, liver disease, history of malignancy in the past 2 years, currently treated of cancer and complex kidney cyst. Medications were dosed to maintain a hemoglobin target between 10 to 11 g/dL. The two primary outcomes were the mean change in the Hb level from baseline to Weeks 28 through 52 and the first occurrence of a major adverse cardiovascular event (MACE; defined as a composite of death from any cause, nonfatal MI, or nonfatal stroke). Daprodustat was shown to be noninferior to rhEPO in the mean change in hemoglobin from baseline to week 28 to 52 (0.3 g/dL versus 0.1 g/dL). The hazard ratio for the time to first occurrence of MACE also met non-inferiority(0.93, 95%

CI, 0.81, 1.07). The most frequently occurring adverse reactions were hypertension, abdominal pain, dizziness, and hypersensitivity.

Daprodustat 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 daprodustat [Jesduvroq] meets the definition of **medical necessity** for when **ALL** of the following are met:

1. Anemia due to chronic kidney disease
    a. Member has been receiving dialysis for at least four 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* or vadadustat (Vafseo)
    h. Dose does not exceed 24 mg daily

Approval duration: 6 months

Continuation of daprodustat [Jesduvroq] 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 vadadustat (Vafseo)
6. Dose does not exceed 24 mg daily

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

Approval duration: 6 months

DOSAGE/ADMINISTRATION:

Adults with Anemia due to CKD receiving dialysis for at least 4 months

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

Adults on dialysis not receiving an ESA:

Pre-treatment Hgb level (g/dL)	Starting dose of daprodustat (Once daily dosing)*
<9	4 mg
<9 to ≤10	2 mg
>10	1 mg

*See prescribing information for dosing if member has hepatic impairment or is taking a moderate CYP2C8 inhibitor

Adults being switched from an ESA:

Current dose of ESA			Dose of Daprodustat*
Epoetin Alfa** (IV units/week)	Darbepoetin Alfa (mcg/4 weeks)	Methoxy PEG-Epoetin Beta (mcg/month)	Once Daily Dosing
Less than or equal to 2,000	20 to 30	30 to 40	4 mg

Greater than 2,000 to less than 10,000	Greater than 30 to 150	Greater than 40 to 180	6 mg
Greater than or equal to 10,000 to less than 20,000	Greater than 150 to 300	Greater than 180 to 360	8 mg
Greater than or equal to 20,000	Greater than 300	Greater than 360	12 mg

*See prescribing information for dosing if member has hepatic impairment or is taking a moderate CYP2C8 inhibitor

**For patients on subcutaneous epoetin alfa, multiply the subcutaneous dose per week by 1.42 to obtain the equivalent IV weekly dose

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 or decrease by one dose level at a time (Dose level: 1 mg, 2 mg, 4 mg, 6 mg, 8 mg, 12 mg, 16 mg, 24 mg). Decrease the dose 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. If hemoglobin exceeds 12 g/dL, interrupt treatment until it returns within target range and then restart at one dose level lower.

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.

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

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

J0899	Daprodustat, 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

Vadadustat (Vafseo), 09-J4000-90

OTHER:

None

REFERENCES:

1. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2023. URL www.clinicalpharmacilogy-ip.com Accessed 06/27/24.

2. Daprodustat (Jesduvroq) [package insert] GlaxoSmithKline, Inc. Durham (NC): August 2023.
3. Micromedex® Healthcare Series [Internet Database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed 06/27/24.

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