Jesduvroq (daprodustat)

NOTICE

This policy contains information which is clinical in nature. The policy is not medical advice. The information in this policy is used by Wellmark to make determinations whether medical treatment is covered under the terms of a Wellmark member's health benefit plan. Physicians and other health care providers are responsible for medical advice and treatment. If you have specific health care needs, you should consult an appropriate health care professional. If you would like to request an accessible version of this document, please contact customer service at 800-524-9242.

BENEFIT APPLICATION

Benefit determinations are based on the applicable contract language in effect at the time the services were rendered. Exclusions, limitations or exceptions may apply. Benefits may vary based on contract, and individual member benefits must be verified. Wellmark determines medical necessity only if the benefit exists and no contract exclusions are applicable. This medical policy may not apply to FEP. Benefits are determined by the Federal Employee Program.

DESCRIPTION

The intent of the Jesduvroq (daprodustat) policy is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. The indications below including FDA-approved indications and compendial uses are considered covered benefits provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Jesduvroq is a hypoxia-inducible factor prolyl hydroxylase (HIF-PH) inhibitor indicated for the treatment of anemia due to chronic kidney disease in adults who have been receiving dialysis for at least four months.

Limitations of Use

- Not been shown to improve quality of life, fatigue, or patient well-being.
- Not indicated for use as a substitute for transfusion in patients requiring immediate correction of anemia
- Not indicated for use in patients not on dialysis

POLICY

Required Documentation

Submission of the following information is necessary to initiate the prior authorization review:

A. Initial Approvals: Chart notes, medical record documentation, and laboratory values (e.g., hemoglobin, ferritin, and transferrin saturation) indicating a diagnosis of anemia due to chronic kidney disease (CKD), duration member has been receiving dialysis, prior treatment (e.g., dose,

frequency, and duration) and responses to erythropoiesis-stimulating agents (ESA) (e.g., epoetin alfa [Epogen, Procrit, Retacrit], darbepoetin alfa [Aranesp], methoxy polyethylene glycol-epoetin beta [Mircera])

B. Continuation Approvals: Recent hemoglobin values (excluding values reflecting recent transfusion)

Prescriber Specialty

This medication must be prescribed by or in consultation with a nephrologist or hematologist

Criteria for Initial Approval

Authorization of 12 weeks may be granted for members with anemia due to chronic kidney disease (CKD) when all of the following criteria are met:

A. Member is 18 years of age or older
B. Member has been receiving dialysis for ≥ 4 months
C. Member has a diagnosis of anemia due to CKD
D. Member has been assessed for iron deficiency anemia and has adequate iron stores OR is receiving iron supplementation prior to starting Jesduvroq
E. Member has a pretreatment hemoglobin level < 11 g/dL (excluding values reflecting recent transfusion)
F. Member is hyporesponsive to erythropoiesis-stimulating agents (ESA) (e.g., epoetin alfa [Epogen, Procrit, Retacrit], darbepoetin alfa [Aranesp], methoxy polyethylene glycol-epoetin beta [Mircera]) when one of the following criteria is met:
    1. Member is requiring >300 IU/kg per week of epoetin alfa
    2. Member is requiring at least 1.5 mcg/kg per week of darbepoetin alfa
G. Member does NOT meet any of the following criteria:
    1. Cardiovascular abnormalities (e.g., myocardial infarction, acute coronary syndrome, stroke, transient ischemic attack) within four weeks of initiation of therapy with the requested drug
    2. History of New York Heart Association (NYHA) Class IV heart failure (refer to Appendix), uncontrolled hypertension, OR liver disease (e.g., ALT >2x ULN, bilirubin >1.5x ULN, current unstable liver disease or biliary disease)
    3. History of malignancy within two years of initiation of therapy with the requested drug, if the member is currently receiving cancer treatment, or if the member has history of a complex kidney cyst
    4. Planned receipt of a living kidney transplant
H. Member will not use the requested drug with an ESA (e.g., epoetin alfa [Epogen, Procrit, Retacrit], darbepoetin alfa [Aranesp], methoxy polyethylene glycol-epoetin beta [Mircera])

Continuation of Therapy

Authorization of 12 weeks may be granted when the following criteria are met:

A. Member has achieved or maintained a clinically meaningful increase in hemoglobin of ≥ 1 g/dL and the member's hemoglobin level is ≤11 g/dL OR the member has not achieved nor maintained a clinically meaningful increase in hemoglobin of ≥ 1 g/dL and ALL the following criteria are met:
    a. The dose will be increased as tolerated to a maximum of 24 mg per day
    b. The member has NOT received 24 mg per day for > 12 weeks without achieving a clinically meaningful increase in hemoglobin of ≥ 1 g/dL
    c. The member's hemoglobin is ≤11 g/dL
B. Member has been assessed for iron deficiency anemia and has adequate iron stores OR is receiving iron supplementation before continuing therapy with Jesduvroq
C. Member will not use the requested drug with an ESA (e.g., epoetin alfa [Epogen, Procrit, Retacrit], darbepoetin alfa [Aranesp], methoxy polyethylene glycol-epoetin beta [Mircera])

Jesduvroq is considered **not medically necessary** for members who do not meet the criteria set forth above.

Other
Requirements regarding current hemoglobin level exclude values due to a recent transfusion.

Dosing and Administration
Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines.

Quantity Limits
Quantities are limited to the FDA approved maximum of 24 mg per day.

APPENDIX

New York Heart Association (NYHA) Functional Classification

Class	Patient Symptoms
I	No limitation of physical activity. Ordinary physical activity does not cause undue fatigue, palpitation, dyspnea (shortness of breath).
II	Slight limitation of physical activity. Comfortable at rest. Ordinary physical activity results in fatigue, palpitation, and dyspnea (shortness of breath).
III	Marked limitation of physical activity. Comfortable at rest. Less than ordinary activity causes fatigue, palpitation, or dyspnea.
IV	Unable to carry on any physical activity without discomfort. Symptoms of heart failure at rest. If any physical activity is undertaken, discomfort increases.

CLINICAL RATIONALE

Anemia of chronic kidney disease (CKD) is a normocytic anemia resulting from an inadequate production of the hormone erythropoietin in the kidneys. Erythropoietin causes the body to produce red blood cells. As CKD advances, the risk of developing anemia increases. Patients with CKD and severe anemia are at risk of complications such as cardiovascular events, increased rates of hospital admissions, cognitive impairment, reduced quality of life, and mortality.

Jesduvroq (daprodustat) is the first FDA approved hypoxia-inducible factor prolyl hydroxylase inhibitor for the treatment of anemia caused by CKD in adults who have received dialysis for a minimum of 4 months. In ASCEND-D, a phase 3, randomized, open-label trial of 2.964 patients, Jesduvroq was shown to be noninferior to erythropoiesis-stimulating agents (ESA) in terms of the primary efficacy and safety outcomes.

The primary efficacy outcome was mean change in hemoglobin from baseline to week 28-52 (non-inferiority margin -0.75 g/dL) and the primary safety outcome was time to first major adverse cardiovascular event (MACE) from day 1 through the end of the study (non-inferiority margin of 1.25). Overall, the mean change in hemoglobin level from baseline to week 28 through 52 was 0.28 g/dL (SD ±0.02 g/dL) in the Jesduvroq treatment arm compared to 0.1 g/dL (SD ±0.02 g/dL) in the ESA treatment arm resulting in a difference of 0.18 g/dL (95% CI 0.12-0.24) which met noninferiority.

Similarly, the proportion of patients with a MACE met noninferiority margins with 25.2% in the Jesduvroq arm versus 26.7% in the ESA arm for a hazard ratio of 0.93 (95% CI 0.81-1.07). Though, due to the significance of the side effects observed, Jesduvroq was assigned a Boxed Warning for increased risk of thrombotic vascular events including death, heart attack, stroke, and blood clots in the lungs, legs, or

dialysis access site. The labeled warnings and precautions also include a risk of hospitalization for heart failure, worsening increase of blood pressure, stomach erosions and gastrointestinal bleeding.

ESAs are the current standard of care for treatment of anemia caused by CKD, but the 2021 Kidney Disease Improving Global Outcomes (KDIGO) guidelines do not recommend one ESA over another. However, 10% of dialysis dependent patients are hyporesponsive to ESAs leaving them without many options. ESAs also carry a Boxed Warning for increased risk serious cardiovascular events, myocardial infarction, stroke, venous thromboembolism, vascular access thrombosis, and mortality when administered to target hemoglobin levels >11 g/dL.

Jesduvroq is an alternative drug therapy for those patients who are hyporesponsive or intolerant to ESAs. Of note, KDIGO guidelines were last published prior to the approval of Jesduvroq, and its use has not been shown to improve quality of life, fatigue, or patient well-being and it is not indicated as a substitute for transfusions or for treatment of anemia of CKD in patients not on dialysis.

PROCEDURES AND BILLING CODES

To report provider services, use appropriate CPT* codes, Alpha Numeric (HCPCS level 2) codes, Revenue codes, and/or ICD diagnostic codes.

- J0889 – daprodustat, oral, 1 mg, (for esrd on dialysis) effective 10/1/23

REFERENCES

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- Singh AK, Blackorby A, Cizman B, et al. Study design and baseline characteristics of patients on dialysis in the ASCEND-D trial. *Nephrol Dial Transplant*. 2022 Apr 25;37(5):960-972. doi: 10.1093/ndt/gfab065.
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POLICY HISTORY

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