Original Effective Date: 03/07/2024
Current Effective Date: 09/15/2024
Last P&T Approval/Version: 07/31/2024
Next Review Due By: 07/2025
Policy Number: C27174-A

Jesduvroq (daprodustat)

PRODUCTS AFFECTED

Jesduvroq (daprodustat)

COVERAGE POLICY

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any. This Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines.

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

DIAGNOSIS:
Anemia associated with chronic kidney disease (CKD) in members on dialysis

REQUIRED MEDICAL INFORMATION:
This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case-by-case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review. When the requested drug product for coverage is dosed by weight, body surface area or other member specific measurement, this data element is required as part of the medical necessity review. The Pharmacy and Therapeutics Committee has determined that the drug benefit shall be a mandatory generic and that generic drugs will be dispensed whenever available.

A. ANEMIA IN CHRONIC KIDNEY DISEASE (CKD):
   1. Documented diagnosis of chronic kidney disease
      AND
   2. Documentation member is receiving dialysis and has been receiving dialysis for at least 4 months

AND

3. (a) Documentation of iron levels (dated within the last 60 days) with the following: Transferrin saturation greater than or equal to 20% AND serum ferritin greater than or equal to 100 ng/mL
   OR
   (b) Prescriber attestation that member is receiving appropriate iron supplementation
   AND
4. Prescriber attests or clinical review has found that any other causes of anemia [i.e., Iron deficiency, underlying infection, or inflammatory process, underlying hematological disease, hemolysis, vitamin deficiencies, blood loss, aluminum intoxication, drug exposure history, gastrointestinal bleeding] have been considered, documented, and corrected (when possible)
   AND
5. Prescriber attests that liver function tests will be assessed prior to initiation of Jesduvroq and monitored during treatment per the FDA label
   AND
6. Documentation hemoglobin (Hgb) level measured within the last two weeks is ≤ 11.5 g/dL
   AND
7. Documentation member is hyporesponsive to erythropoietin stimulating agents (ESA)
   NOTE: ESA hyporesponsiveness generally refers to inability to achieve desired hemoglobin levels despite higher than usual ESA doses
   MOLINA REVIEWER NOTE: Review preferred ESA status if available
   AND
8. Prescriber attests to (or the clinical reviewer has found that) the member not having any FDA labeled contraindications that haven't been addressed by the prescriber within the documentation submitted for review [Contraindications to Jesduvroq (daprodustat) include: patients receiving a strong CYP2C8 inhibitor such as gemfibrozil, patients with uncontrolled hypertension]

CONTINUATION OF THERAPY:

A. ANEMIA IN CHRONIC KIDNEY DISEASE (CKD):
   1. Adherence to therapy at least 85% of the time as verified by the prescriber or member medication fill history OR adherence less than 85% of the time due to the need for surgery or treatment of an infection, causing temporary discontinuation
      AND
   2. Documentation recent hemoglobin is < 11 g/dL [DOCUMENTATION REQUIRED]
      NOTE: Do not target a hemoglobin higher than 11 g/dL.
      AND
   3. Documentation recent transferrin saturation greater than or equal to 20% or serum ferritin greater than or equal to 100 ng/mL or member is receiving appropriate iron supplementation
      AND
   4. Documented improvement in hematocrit and hemoglobin levels have occurred or there is a significant decrease in transfusion requirements
      NOTE: Treatment with Jesduvroq should not be continued beyond 24 weeks of therapy if a clinically meaningful increase in hemoglobin level is not achieved. Alternative explanations for an inadequate response should be sought and treated before re-starting therapy.
      AND
   5. Prescriber attests to monitoring liver function tests as needed per FDA label
      AND
   6. Prescriber attests to or clinical reviewer has found no evidence of intolerable adverse effects or drug toxicity

DURATION OF APPROVAL:

Initial authorization: 6 months, Continuation of Therapy: 12 months

PRESCRIBER REQUIREMENTS:
Prescribed by or in consultation with a board-certified nephrologist [If prescribed in consultation, consultation notes must be submitted with initial request and reauthorization requests]

AGE RESTRICTIONS:
18 years of age and older

QUANTITY:
Member not being treated with an ESA:
Dose based on pre-treatment hemoglobin level
< 9 g/dL: 4mg once daily
≥ 9 g/dL to ≤ 10 g/dL: 2mg once daily
> 10 g/dL: 1 mg once daily

Member switching from an ESA:

Current Dose of ESA			Dose of Jesduvroq
Epoetin Alfa IV (units/week)	**Darbepoetin Alfa SQ/IV (mcg/4 weeks)**	**Methoxy PEG-Epoetin Beta SQ/IV (mcg/month)**	**Once Daily Dosing**
≤ 2000	20 to 30	30 to 40	4 mg
> 2000 to < 10000	> 30 to 150	> 40 to 180	6 mg
≥ 10000 to < 20000	> 150 to 300	> 180 to 360	8 mg
≥ 20000	> 300	> 360	12 mg

Maximum Quantity Limits – 24 mg once daily

PLACE OF ADMINISTRATION:
The recommendation is that oral medications in this policy will be for pharmacy benefit coverage and patient self-administered.

DRUG INFORMATION

ROUTE OF ADMINISTRATION:
Oral

DRUG CLASS:
Hypoxia-inducible Factor Prolyl Hydroxylase Inhibitor

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

COMPENDIAL APPROVED OFF-LABELED USES:
None

APPENDIX

APPENDIX:
None

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:
Jesduvroq (daprodustat) is the first approved oral treatment for anemia in CKD in adults on dialysis. It is a hypoxia-inducible factor prolyl hydroxylase (HIF-PH) inhibitor, a new class of medications developed to stimulate the transcription of the erythropoietin gene, leading to increased levels of endogenous erythropoietin. They may also improve iron mobilization to the bone marrow and can possibly decrease the use of IV iron in patients with ESRD.

Erythropoietin-stimulating agents (ESAs) are the current standard of care for treating anemia in CKD, but they are largely reserved for the dialysis dependent population given their parenteral administration, storage requirements, and cardiovascular safety concerns.

Approval of Jesduvroq was based on the ASCEND-D trial. ASCEND-D was a Phase 3, global, randomized, open-label, parallel-group, active-controlled, event-driven trial evaluating the efficacy and safety of Jesduvroq in patients with anemia due to CKD on dialysis and who were being treated with an ESA. Prior ESAs were continued during the screening and run-in periods. Patients were randomized to Jesduvroq or recombinant human erythropoietin. Patients on hemodialysis and peritoneal dialysis were included in the study. The efficacy and safety of Jesduvroq were evaluated as co-primary endpoints: the mean change in hemoglobin from baseline to the Evaluation Period (Weeks 28 to 52) and time to first adjudicated MACE (defined as all-cause mortality, non-fatal myocardial infarction, or non-fatal stroke), using a non-inferiority comparison to rhEPO (epoetin alfa and darbepoetin alfa) for both endpoints. The lower limit of the 95% confidence interval (CI) for the overall hemoglobin treatment difference was greater than the pre-specified non-inferiority margin of -0.75 g/dL, demonstrating non-inferiority of Jesduvroq to rhEPO with respect to the mean change in hemoglobin between baseline and over the Evaluation Period. The hazard ratio for the time to first occurrence of MACE, a composite of all-cause mortality, non-fatal myocardial infarction, and non-fatal stroke, comparing Jesduvroq to rhEPO was 0.93 (95% CI 0.81, 1.07) (Table 7). Non-inferiority of Jesduvroq to rhEPO on MACE was achieved because the upper limit of the 95% CI for the MACE hazard ratio was less than the pre-specified non-inferiority margin of 1.25.

Permanent treatment discontinuation due to an adverse reaction was reported in 19% of patients treated with Jesduvroq and 18% of patients treated with rhEPO. No specific adverse reaction resulted in permanent treatment discontinuation in >1% of patients treated with Jesduvroq. The most common adverse reactions (≥10% of Jesduvroq-treated patients) were hypertension, thrombotic vascular events, and abdominal pain. Adjudicated thrombotic vascular events (fatal and non-fatal) were observed in 9.8 per 100 PY of patients receiving Jesduvroq and in 11.7 per 100 PY of patients receiving rhEPO.

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:
All other uses of Jesduvroq (daprodustat) are considered experimental/investigational and therefore, will follow Molina's Off- Label policy. Contraindications to Jesduvroq (daprodustat) include: patients receiving a strong CYP2C8 inhibitor such as gemfibrozil, patients with uncontrolled hypertension.

OTHER SPECIAL CONSIDERATIONS:
Jesduvroq (daprodustat) has a BLACK BOX WARNING for increased risk of death, myocardial infarction, stroke, venous thromboembolism, and thrombosis of vascular access. Jesduvroq increases the risk of thrombotic vascular events, including major adverse cardiovascular events. 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 (ESAs), which also increase erythropoietin levels. No trial has identified a hemoglobin target level, dose of Jesduvroq, or dosing strategy that does not increase these risks. Use the lowest dose of Jesduvroq sufficient to reduce the need for red blood cell transfusions.

Jesduvroq should be swallowed whole. Tablets should not be cut, crushed, or chewed. Jesduvroq can be

administered without regard to the timing or type of dialysis. If a dose of Jesduvroq is missed, it should be taken as soon as possible, unless it is the same day as the next dose. In this case, the missed dose should be skipped, and the next dose taken at the usual time. Double doses should not be taken to make-up for a missed dose.

CODING/BILLING INFORMATION

Note: 1) This list of codes may not be all-inclusive. 2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement

HCPCS CODE	DESCRIPTION
J0889	Daprodustat, oral, 1 mg, (for esrd on dialysis)

AVAILABLE DOSAGE FORMS:
Jesduvroq TABS 1MG
Jesduvroq TABS 2MG
Jesduvroq TABS 4MG
Jesduvroq TABS 6MG
Jesduvroq TABS 8MG

REFERENCES

1. Jesduvroq (daprodustat) tablets, for oral use [prescribing information]. Durham, NC: GlaxoSmithkline; August 2023.
2. Kidney Disease: Improving Global Outcomes (KDIGO). (2012). Official journal of the international society of nephrology. KDIGO Clinical Practice Guideline for Anemia in Chronic Kidney Disease. Retrieved from https://kdigo.org/wp-content/uploads/2016/10/KDIGO-2012-Anemia-Guideline-English.pdf
3. Natale, P., Palmer, S. C., Jaure, A., Hodson, E. M., Ruospo, M., Cooper, T. E., … Strippoli, G. F. (2022). Hypoxia-inducible factor stabilisers for the anaemia of chronic kidney disease. Cochrane Database of Systematic Reviews, 2022(8). https://doi.org/10.1002/14651858.cd013751.pub2
4. Singh, A. K., Carroll, K., Perkovic, V., Solomon, S., Jha, V., Johansen, K. L., … Meadowcroft, A. M. (2021). Daprodustat for the Treatment of Anemia in Patients Undergoing Dialysis. New England Journal of Medicine, 385(25), 2325–2335. https://doi.org/10.1056/nejmoa2113379

SUMMARY OF REVIEW/REVISIONS	DATE
REVISION- Notable revisions: Coding/Billing Information	Q3 2024
NEW CRITERIA CREATION	Q1 2024