daprodustat (Jesduvroq™)

Policy # 00868
Original Effective Date: 04/08/2024
Current Effective Date: 04/08/2024

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider daprodustat (Jesduvroq™)‡ for the treatment of anemia due to chronic kidney disease to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility for daprodustat (Jesduvroq) for the treatment of anemia due to chronic kidney disease will be considered when the following criteria are met:

- Initial
    - Patient is greater than or equal to 18 years of age; AND
    - Patient has a diagnosis of anemia due to chronic kidney disease; AND
    - Patient has been receiving dialysis for greater than or equal to 4 months; AND
    - Patient has adequate iron stores as evidenced by a transferrin saturation of at least 20% and/or ferritin of at least 100 ng/mL; AND
    - Patient's hemoglobin level is less than or equal to 11 g/dL; AND
    - Patient does NOT have any cardiovascular comorbidities (e.g., myocardial infarction, acute coronary syndrome, stroke, or transient ischemic attack within 4 weeks of screening, New York Heart Association Class IV heart failure, uncontrolled hypertension); AND
      *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
    - Requested drug will NOT be used in combination with an erythropoiesis stimulating agent (ESA) such as epoetin alfa (Epogen®, Procrit®)‡, darbepoetin alfa (Aranesp®)‡, or pegylated epoetin beta (Mircera®)‡.

*(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*

- Continuation
  - Patient has received an initial authorization for Jesduvroq; AND
  - Requested drug will NOT be used in combination with an erythropoiesis stimulating agent (ESA) such as epoetin alfa (Epogen, Procrit), darbepoetin alfa (Aranesp), or pegylated epoetin beta (Mircera); AND
    *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
  - Provider attests that the patient has experienced improvement on treatment. Examples of improvement with Jesduvroq include decreased need for RBC transfusion and increased hemoglobin levels.
    *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*

When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the use of daprodustat (Jesduvroq) in patients with cardiovascular comorbidities or in combination with an ESA to be **not medically necessary.****

Based on review of available data, the Company considers the use of continued use of daprodustat (Jesduvroq) when the patient has not experienced improvement on treatment to be **not medically necessary.****

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of daprodustat (Jesduvroq) when patient selection criteria are not met (except those denoted above as **not medically necessary****) to be **investigational.***

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Background/Overview

Jesduvroq is a reversible inhibitor of hypoxia-inducible factor prolyl hydroxylase inhibitor indicated for the treatment of anemia due to chronic kidney disease (CKD) in adults who have been receiving dialysis for at least 4 months. It works by stabilizing and causing the accumulation of certain hypoxia-inducible transcription factors that ultimately leads to the increased production of erythropoietin and red blood cells. Jesduvroq is dosed orally once daily with dosing individualized and titrated based on the hemoglobin level and response to therapy. As with erythropoiesis stimulating agents (ESAs), a hemoglobin level of >11 g/dL should NOT be targeted. The lowest dose needed to reduce the need for red blood cell (RBC) transfusions should be used. Additionally, Jesduvroq use should not be continued beyond 24 weeks if a clinically meaningful increase in hemoglobin is not achieved. Jesduvroq has a boxed warning regarding an increased risk of death, myocardial infarction, stroke, venous thromboembolism, and thrombosis of vascular access. Additionally, it is contraindicated in patients with uncontrolled hypertension.

CKD is estimated to impact more than 1 in 7 US adults and is often caused by the chronic conditions of diabetes and hypertension. Once CKD progresses to end stage renal disease (ESRD), treatment options are limited to dialysis or kidney transplantation. Anemia is a common complication in patients with CKD caused by erythropoietin deficiency and reduced renal production of erythropoietin. An impaired ability to absorb and utilize stored iron is also a factor. Treatment options for this anemia include iron therapy, RBC transfusions, and erythropoietin stimulating agents (ESAs) such as epoetin alfa (Epogen, Procrit, Retacrit), darbepoetin alfa (Aranesp), and pegylated epoetin beta (Mircera). Jesduvroq represents the first oral agent that works to stimulate RBC production. Clinical practice guidelines have not been updated to include Jesduvroq.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Jesduvroq was approved in February 2023 for the treatment of anemia due to chronic kidney disease in adults who have been receiving dialysis for at least four months.

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Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

The efficacy and safety of Jesduvroq were evaluated in 2,964 adults with anemia due to CKD on dialysis and receiving an ESA at the time of study entry in a randomized, sponsor-blind, active-controlled, global, multicenter, event-driven clinical trial. Patients were stratified by dialysis type and were required to be on dialysis for at least 4 months prior to the first dose of Jesduvroq. Patients on hemodialysis were randomized 1:1 to receive oral Jesduvroq (n=1,316) or intravenous epoetin alfa (n=1,308) while patients on peritoneal dialysis were randomized 1:1 to receive oral Jesduvroq (n=171) or subcutaneous darbepoetin alfa (n=169).

Key exclusion criteria included: ferritin $\leq$100 ng/mL, transferrin saturation $\leq$20% at screening, evidence of non-renal anemia, cardiovascular abnormalities (including myocardial infarction, acute coronary syndrome, stroke or transient ischemic attack within 4 weeks of screening, NYHA Class IV heart failure, and uncontrolled hypertension), liver disease, history of malignancy within 2 years of screening, current treatment of cancer, and complex kidney cyst.

Dosing in each treatment arm followed a protocol-specified adjustment algorithm to achieve and/or maintain a hemoglobin target of 10 to 11 g/dL. Patients receiving other ESAs were switched to the epoetin alfa or darbepoetin alfa equivalent starting dose.

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 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. Results were similar in patients receiving either hemodialysis or peritoneal

dialysis. Regarding safety, 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). 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.

References

1. Jesduvroq [package insert]. GlaxoSmithKline LLC. Durham, NC. Updated August 2023.
2. Jesduvroq Drug Evaluation. Express Scripts. Updated February 2023.

Policy History

Original Effective Date: 04/08/2024
Current Effective Date: 04/08/2024
03/07/2024 Medical Policy Committee review
03/13/2024 Medical Policy Implementation Committee approval. New policy.
Next Scheduled Review Date: 03/2025

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:

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1. Consultation with technology evaluation center(s);
2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
3. Reference to federal regulations.

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: If the Patient's health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

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NOTICE: Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage.