PHARMACY COVERAGE GUIDELINE

JESDUVROQ (daprodustat) oral
VAFSEO® (vadadustat) oral
Generic Equivalent (if available)

This Pharmacy Coverage Guideline (PCG):
- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively "Service") is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider's judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member's benefit plan; and
- Is subject to change as new information becomes available.

Scope
- This PCG applies to Commercial and Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

Instructions & Guidance
- To determine whether a member is eligible for the Service, read the entire PCG.
- This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
- Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
- The "Criteria" section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member's benefit plan.
- The "Description" section describes the Service.
- The "Definition" section defines certain words, terms or items within the policy and may include tables and charts.
- The "Resources" section lists the information and materials we considered in developing this PCG
- **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
- Information about medications that require prior authorization is available at www.azblue.com/pharmacy. You must fully complete the request form and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to Pharmacyprecert@azblue.com.

Criteria:

➢ **Criteria for initial therapy:** Jesduvroq (daprodustat), Vafseo (vadadustat), and/or generic equivalent (if available) is considered ***medically necessary*** and will be approved when **ALL** the following criteria are met:

1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with a Nephrologist
2. Individual is 18 years of age or older
3. Individual has a confirmed diagnosis of anemia due to chronic kidney disease (CKD)
4. Individual is **ONE** of the following:
    a. **For Jesduvroq:** Has been receiving dialysis for at least four months

b. **For Vafseo:** Has been receiving dialysis for at least three months

5. Individual has received and completed **ALL** the following **baseline tests** before initiation of treatment and with continued monitoring of the individual as clinically appropriate:
    a. Evaluation of iron stores (e.g., serum ferritin, percent transferrin saturation, serum iron) reveal adequate iron
    b. Serum alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase, and total bilirubin
    c. Hemoglobin level is less than 11 g/dL

6. **If available:** Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

7. Individual has documented failure (after at least 6 weeks), contraindication per FDA label, intolerance, or is not a candidate for **TWO** of the following:
    a. Erythropoietin (Epoetin, Procrit, etc.)
    b. Darbepoetin (Aranesp)
    c. Methoxy Polyethylene Glycol Epoetin Beta (Mircera)

8. There are **NO** FDA-label contraindications such as:
    a. **For Jesduvroq and Vafseo:** Uncontrolled hypertension
    b. **Additional for Jesduvroq:** Concurrent use of strong cytochrome P450 2C8 (CYP2C8) inhibitors such as gemfibrozil

9. Individual does not have the following:
    a. **For both Jesduvroq and Vafseo:**
        i. Kidney transplant
        ii. Non-renal anemias such as aplasias, untreated pernicious anemia, thalassemia major, sickle cell disease, myelodysplastic syndrome, or GI bleed
        iii. Active malignancy
        iv. History of myocardial infarction, acute coronary syndrome, cerebrovascular event
        v. Anemia due to acute blood loss
    b. **Additional for Jesduvroq:**
        i. New York Heart Association (NYHA) Class IV heart failure
        ii. Severe hepatic impairment (Child-Pugh Class C)
    c. **Additional for Vafseo:**
        i. Cirrhosis or active, acute liver disease

10. Requested agent will not be approved if iron stores are inadequate

11. Requested agent will not be approved if individual with chronic kidney disease is not receiving dialysis

12. Requested agent will not be used in combination with an erythropoiesis-stimulating agent (ESA) (e.g., Epoetin, Procrit, Aranesp, Mircera, etc.)

Initial approval duration: 6 months
Note: Treatment with should not be continued beyond 6 months of therapy if a clinically meaningful increase in Hb level is not achieved

- **Criteria for continuation of coverage (renewal request):** Jesduvroq (daprodustat), Vafseo (vadadustat), and/or generic equivalent (if available) is considered ***medically necessary*** and will be approved when **ALL** the following criteria are met **(samples are not considered for continuation of therapy)**:

1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation with a Nephrologist

2. Individual's condition has responded while on therapy with response defined as **BOTH** of the following:
    a. Hemoglobin is within target range of 10-11 g/dL
    b. There is a reduction in need for red blood cell transfusions

3. Individual has been adherent with the medication

4. **If available:** Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

5. Individual has not developed any contraindications or other significant adverse drug effects that may exclude continued use such as:
    a. **For both Jesduvroq and Vafseo:**
        i. Worsening hypertension or hypertensive crisis
        ii. Hypertensive encephalopathy
        iii. Seizure
        iv. Gastric or esophageal erosion
        v. Gastrointestinal bleeding
        vi. Myocardial Infarction
        vii. Stroke
        viii. Arterial or venous thromboembolism
        ix. Thrombosis of vascular access
    b. **Additional for Jesduvroq:** Heart failure
    c. **Additional for Vafseo:** Persistently elevated ALT or AST or if accompanied by elevated bilirubin

6. Individual does not have the following:
    a. **For both Jesduvroq and Vafseo:**
        i. Kidney transplant
        ii. Non-renal anemias such as aplasia, untreated pernicious anemia, thalassemia major, sickle cell disease, myelodysplastic syndrome, or GI bleed
        iii. Active malignancy
        iv. History of myocardial infarction, acute coronary syndrome, cerebrovascular event
        v. Anemia due to acute blood loss
    b. **Additional for Jesduvroq:**

i. New York Heart Association (NYHA) Class IV heart failure
ii. Severe hepatic impairment (Child-Pugh Class C)

c. **Additional for Vafseo:**
i. Cirrhosis or active, acute liver disease

7. Requested agent will not be approved if iron stores are inadequate

8. Requested agent will not be approved if individual with chronic kidney disease is not receiving dialysis

9. Requested agent will not be used in combination with an erythropoiesis-stimulating agent (ESA) (e.g., Epoetin, Procrit, Aranesp, Mircera, etc.)

Renewal duration: 12 months

- Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

1. **Off-Label Use of Non-Cancer Medications**

2. **Off-Label Use of Cancer Medications**

Description:

Jesduvroq (daprodustat) is a hypoxia-inducible factor prolyl hydroxylase inhibitor (HIF PHI) indicated for the treatment of anemia due to chronic kidney disease (CKD) in adults who have been receiving dialysis for at least four months. Jesduvroq (daprodustat) has not been shown to improve quality of life, fatigue, or patient well-being. Jesduvroq (daprodustat) is not indicated for use as a substitute for red blood cell transfusions in patients who require immediate correction of anemia, and it is not indicated for treatment of anemia of CKD in patients who are not on dialysis.

Vafseo (vadadustat) is a hypoxia-inducible factor prolyl hydroxylase (HIF PH) inhibitor indicated for the treatment of anemia due to chronic kidney disease (CKD) in adults who have been receiving dialysis for at least three months. Vafseo (vadadustat) has not been shown to improve quality of life, fatigue, or patient well-being. Vafseo (vadadustat) is not indicated for use as a substitute for red blood cell transfusions in patients who require immediate correction of anemia, and it is not indicated for treatment of anemia of CKD in patients who are not on dialysis.

Anemia occurs in chronic kidney disease (CKD); it is more common as kidney function declines. The anemia is associated with increased morbidity and mortality related to cardiovascular (CV) disease and an increased risk of hospitalization. Established treatments include erythropoiesis-stimulating agents (ESAs), iron supplementation and blood transfusions. Oral hypoxia-inducible factors (HIF) stabilizers are another option available to manage anemia in people with CKD.

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Screening for and treating anemia is routine care of patients on hemodialysis. Anemia is defined by World Health Organization (WHO) as a hemoglobin (Hb) concentration <13 g/dL for adult males and postmenopausal females and an Hb concentration <12 g/dL for premenopausal females. The optimal target Hb for patients treated with an Erythropoiesis-Stimulating Agent (ESA) or an HIF PHI is not known. In most patients on dialysis who are treated with ESAs or HIF PHIs, Hb levels are maintained between 10 and 11 g/dL. Target Hb concentrations >12 g/dL should be avoided.

Among patients on hemodialysis, the goals of use ESAs or HIF PHI is to avoid severe anemia and reduce the need for blood transfusions but not to normalize Hb levels. Multiple studies have shown that, among patients with CKD (including those on hemodialysis), correcting Hb to normal increases the risk of adverse outcomes. Evaluation of anemia should include red blood cell indices, reticulocyte count, serum iron, total iron-binding capacity (TIBC), percent transferrin saturation (TSAT= plasma iron divided by TIBC x 100), serum ferritin, serum folate and vitamin B12 levels, and testing for occult blood in stool.

Definitions:

U.S. Food and Drug Administration (FDA) MedWatch Forms for FDA Safety Reporting
MedWatch Forms for FDA Safety Reporting | FDA

Resources:

Jesduvroq (daprodustat) product information, revised by GlaxoSmithKline LLC 08-2023. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed August 26, 2024.

Vafseo (vadadustat) product information, revised by Akebia Therapeutics, Inc. 03-2024. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed August 26, 2024.

Berns JS. Diagnosis of iron deficiency in chronic kidney disease. In: UpToDate, Golper TA, Taylor EN (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through September 2024. Topic last updated March 12, 2024. Accessed October 02, 2024.

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Berns JS, Qunibi WY. Treatment of anemia in patients on dialysis. In: UpToDate, Schwab SJ, Curhan GC, Taylor EN (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through September 2024. Topic last updated April 30, 2024. Accessed October 02, 2024.

Natale P, Palmer SC, Jaure A, et al.: Hypoxia-inducible factor stabilizers for the anemia of chronic kidney disease (Review). Cochrane Database Syst Rev. 2022 Aug 25;8(8):CD013751. DOI: 10.1002/14651858.CD013751.pub2. Accessed November 10, 2023. Re-evaluated October 02, 2024.

Eckardt KU, Agarwal R, Aswad A, et al,: Safety and Efficacy of Vadadustat for Anemia in Patients Undergoing Dialysis. NEJM 2021 April 29;384 (17):1601-1612. Accessed July 28, 2024. Re-evaluated October 02, 2024.

Singh AK, Carroll K, Perkovic V, et. al.: Daprodustat for the Treatment of Anemia in Patients Undergoing Dialysis. NEJM 2021 Dec 16;385:2325-2335. DOI: 10.1056/NEJMoa2113379. Accessed November 10, 2023. Re-evaluated October 02, 2024.

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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. Accessed November 10, 2023. Re-evaluated October 02, 2024.