Policy and Procedure	
PHARMACY PRIOR AUTHORIZATION AND STEP THERAPY POLICY AND CRITERIA ORPTCHEM043.1024	**HEMATOLOGICAL AGENT** **JESDUVROQ®** (daprodustat tablet) **VAFSEO®** (vadadustat tablet)
Effective Date: 01/01/2025	**Review/Revised Date**: 10/24 (SNM)
Original Effective Date: 06/24	**P&T Committee Meeting Date**: 04/24, 10/24
Approved by: Oregon Region Pharmacy and Therapeutics Committee	

SCOPE:
Providence Health Plan, Providence Health Assurance, Providence Plan Partners, and Ayin Health Solutions as applicable (referred to individually as "Company" and collectively as "Companies").

APPLIES TO:
Medicare Part B

POLICY CRITERIA:

COVERED USES:
All Food and Drug Administration (FDA)-Approved Indications

REQUIRED MEDICAL INFORMATION:
For initial authorization, all the following must be met:
1. Documentation of anemia due to chronic kidney disease (CKD)
2. Documentation that the patient has received dialysis as outlined:
    a. For Jesduvroq®: Has received dialysis for at least four months
    b. For Vafseo®: Has received dialysis for at least three months
3. Adequate iron stores as indicated by current (within the last three months) serum ferritin level greater than or equal to 100 mcg/L or serum transferrin saturation greater than or equal to 20%
4. Documentation that the patient is hyporesponsive to erythropoiesis-stimulating agent therapy

For patients established on the requested medication (within the previous year), all the following must be met:
1. Documentation of anemia due to CKD
2. Documentation the patient has experienced a therapeutic response, defined by an increase in hemoglobin from baseline

EXCLUSION CRITERIA:

- For Jesduvroq®: Concomitant use of strong CYP2C8 inhibitors (such as gemfibrozil)
- Uncontrolled hypertension

AGE RESTRICTIONS:
May be approved for patients aged 18 years and older

PRESCRIBER RESTRICTIONS:
Must be prescribed by, or in consultation with, a nephrologist or hematologist.

COVERAGE DURATION:
Initial authorization and reauthorization will be approved for one year.

Requests for indications that were approved by the FDA within the previous six (6) months may not have been reviewed by the health plan for safety and effectiveness and inclusion on this policy document. These requests will be reviewed using the New Drug and or Indication Awaiting P&T Review; Prior Authorization Request ORPTCOPS047.

Requests for a non-FDA approved (off-label) indication requires the proposed indication be listed in either the American Hospital Formulary System (AHFS), Drugdex, or the National Comprehensive Cancer Network (NCCN) and is considered subject to evaluation of the prescriber's medical rationale, formulary alternatives, the available published evidence-based research and whether the proposed use is determined to be experimental/investigational.

Coverage for Medicaid is limited to a condition that has been designated a covered line item number by the Oregon Health Services Commission listed on the Prioritized List of Health Care Services.

Coverage decisions are made on the basis of individualized determinations of medical necessity and the experimental or investigational character of the treatment in the individual case.

INTRODUCTION:
Daprodustat is the first in its class, HIP-PH inhibitor, to be approved by the FDA.

FDA APPROVED INDICATIONS:
Daprodustat (Jesduvroq®) is indicated for the treatment of anemia due to chronic kidney disease (CKD) in adults who have been receiving dialysis for at least four months. Limitations of use: Daprodustat has not been shown to improve quality of life, fatigue, or patient well-being; daprodustat is not indicated for use: as a substitute for red blood cell transfusions in patients who require immediate correction of anemia, or for treatment of anemia of chronic kidney disease in patients who are not on dialysis.

Vadadustat (Vafseo®) is indicated for the treatment of anemia due to chronic kidney disease (CKD) in adults who have been receiving dialysis for at least three months. Limitations of use: Vadadustat has not been shown to improve quality of life, fatigue, or patient well-being; vadadustat is not indicated for use: as a substitute for red blood cell transfusions in patients who require immediate correction of anemia, in patients with anemia due to CKD not on dialysis.

POSITION STATEMENT:

Daprodustat

Daprodustat is FDA approved based on one phase 3, global, randomized, open-label, parallel-group, active-controlled, event-driven trial (ASCEND-D) evaluating daprodustat in adults with dialysis-dependent CKD with anemia. Daprodustat was found to be non-inferior to erythropoiesis-stimulating agent (ESA) therapy (epoetin or darbepoetin) (n=1,474) regarding time to first occurrence of a major cardiovascular event (MACE). Patients in the clinical trial were required to have anemia related to CKD, a serum ferritin level > 100 ng/mL, and a TSAT > 20%. Patients with a recent cardiovascular event or current or recent cancer were excluded. Patients were randomized 1:1 to receive oral daprodustat (n=1,937) once daily or SC darbepoetin alfa (n=1,935) once weekly, once every two weeks, or once every four weeks.

- Results of coprimary outcomes:
    - Mean change in Hb from baseline to the average during the primary evaluation period (weeks 28 through 52), assessed for noninferiority.
    - Mean change in Hb was 0.74 +0.02 g/dL with daprodustat and 0.66 +0.02 g/dL with darbepoetin for a difference of 0.08 g/dL (95% CI, 0.03 to 0.13) which met the prespecified noninferiority margin.
    - First occurrence of an adjudicated MACE, a composite of death from any cause, nonfatal MI, or nonfatal stroke, assessed for noninferiority. A first MACE was reported in 19.5% of patients in the daprodustat group and 19.2% of patients in the darbepoetin group meeting the prespecified noninferiority margin of 1.25 (HR, 1.03; 95% CI, 0.89 to 1.19).
    - An on-treatment MACE analysis which censored data on patients at 28 days after the date of the last dose demonstrated a higher incidence of first MACE with daprodustat (14.1%) versus darbepoetin (10.5%) (HR, 1.4; 95% CI, 1.17 to 1.68).
- Safety Outcomes:
    - In both treatment groups, hypertension was the most commonly reported adverse event (13% in the daprodustat group, 14% in the darbepoetin group). Treatment-emergent serious adverse events, including pneumonia, acute kidney injury, acute MI, and azotemia, occurred in 43.9% of daprodustat-treated patients and 36.4% of ESA-treated patients. Esophageal or gastric erosions (3.6% versus 2.1%; p=0.005) and cancer-

related death or tumor progression/recurrence (3.7% versus 2.5%; p=0.04) occurred more frequently with daprodustat.

Daprodustat is unique compared to ESA therapy as daprodustat is administered by mouth in a tablet formulation while ESA therapy are injections. Additionally, daprodustat is taken daily while ESA therapy is commonly administered on a weekly basis (such as three times a week, once a week, or once every couple of weeks). Guideline guidance for daprodustat is not available. NICE guidelines are in development for daprodustat for treating anemia in people with chronic kidney disease.

Safety for daprodustat includes:

- Boxed warning includes increased risk of death, myocardial infarction, stroke venous thromboembolism and thrombosis of vascular access
- Warnings and precautions include increased risk of death, myocardial infarction, stroke, venous thromboembolism, and thrombosis of vascular access; risk of hospitalization for heart failure; hypertension; gastrointestinal erosion; serious adverse events in patients with anemia due to chronic kidney disease and not on dialysis; malignancy
- Contraindications include concomitant use of strong CYP2C8 inhibitors, uncontrolled hypertension
- Common adverse events include abdominal pain (11%), hypersensitivity reaction (7%), and dizziness (7%)

Vadadustat

Vadadustat efficacy is established in two phase 3, active-controlled, non-inferiority trials that vadadustat improves and maintains hemoglobin levels in adults with CKD on dialysis; results from both trials showed that vadadustat was non-inferior to darbepoetin alfa.

Vadadustat is the second oral HIF-PH inhibitor approved for the treatment of anemia due to CKD in adult patients on dialysis; in February 2023 daprodustat was approved for the same indication in adults who have been receiving dialysis for at least four months.

Boxed warnings included increased risk of death, myocardial infarction, stroke, venous thromboembolism and thrombosis of vascular access. Contraindications include uncontrolled hypertension. Vadadustat does not carry increased risk of hospitalization for heart failure as other HIF-PH inhibitor, daprodustat. Other warnings and precautions include hepatotoxicity, hypertension, seizures, gastrointestinal erosion, malignancy, adverse reactions in patients not on dialysis.

Common adverse reactions occurring in greater than 5% of patients include hypertension, diarrhea, headache, nausea, fatigue, abdominal pain, vomiting, gastrointestinal erosion, dizziness, dyspnea, arteriovenous fistula thrombosis, dialysis related complication.

BILLING GUIDELINES AND CODING:

CODES*		
HCPCS	J0889	Daprodustat, oral, 1 mg, (for esrd on dialysis)
	J0901	Vadadustat, oral, 1 mg (for esrd on dialysis)

*Coding Notes:
• The above code list is provided as a courtesy and may not be all-inclusive. Inclusion or omission of a code from this policy neither implies nor guarantees reimbursement or coverage. Some codes may not require routine review for medical necessity, but they are subject to provider contracts, as well as member benefits, eligibility and potential utilization audit.
• HCPCS/CPT code(s) may be subject to National Correct Coding Initiative (NCCI) procedure-to-procedure (PTP) bundling edits and daily maximum edits known as “medically unlikely edits” (MUEs) published by the Centers for Medicare and Medicaid Services (CMS). This policy does not take precedence over NCCI edits or MUEs. Please refer to the CMS website for coding guidelines and applicable code combinations.

REFERENCE/RESOURCES:

1. Daprodustat (Jesduvroq®) package insert. Emeryville, CA. Santen Incorporated. October, 2023.
2. Daprodustat In: DRUGDEX® System [Internet database]. Greenwood Village, Colo: Thomson Reuters (Healthcare) Inc. Updated periodically. Accessed March 1, 2024.
3. Daprodustat In: Lexi-Drugs Online [Internet database]. Hudson, OH: Lexi-Comp, Inc. Updated periodically. Accessed March 1, 2024.
4. Jesduvroq (daprodustat) tablets monograph. Prime Therapeutics. November 30, 2024.
5. Vadadustat (Vafseo®) Package insert. Cambridge, MA: Akebia Therapeutics, Inc; June 2024.
6. Vadadustat In: DRUGDEX® System [Internet database]. Greenwood Village, Colo: Thomson Reuters (Healthcare) Inc. Updated periodically. Accessed August 23, 2024
7. Vadadustat In: Lexi-Drugs Online [Internet database]. Hudson, OH: Lexi-Comp, Inc. Updated periodically. Accessed August 23, 2024
8. Eckardt KU, et al. Global Phase 3 programme of vadadustat for treatment of anaemia of chronic kidney disease: rationale, study design and baseline characteristics of dialysis dependent patients in the INNO2VATE trials. Nephrol Dial Transplant. 2021;36(11):2039– 2048.
9. Eckardt KU, et al. Safety and efficacy of vadadustat for anemia in patients undergoing dialysis. N Engl J Med. 2021;384(17):1601–1612.