Original Effective Date: 12/06/2024
Current Effective Date: 12/06/2024
Last P&T Approval/Version: 10/30/2024
Next Review Due By: 07/2025
Policy Number: C28641-A

Vafseo (vadadustat)

PRODUCTS AFFECTED

Vafseo (vadadustat)

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 with 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 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 for

REQUIRED MEDICAL INFORMATION:
This clinical policy is consistent with standards of medical practice current when it 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. More information may be required case-by-case 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 3 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 Vadadustat, monthly after initiation for the first 6 months, and then monitor as clinically indicated 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 Vafseo (vadadustat) include: known hypersensitivity to Vafseo or any of its components, and 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 Vadadustat should not be continued beyond 24 weeks (about 5 and a half months) 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: Starting dose 300 mg by mouth once daily
Member switching from an ESA: Starting dose: 300 mg by mouth once daily
See Appendix

Maximum Quantity Limits – 600 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 (HIF-PHI)

FDA-APPROVED USES:
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: 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 or in patients with anemia due to CKD not on dialysis.

COMPENDIAL APPROVED OFF-LABELED USES:
None

APPENDIX

APPENDIX:
Member not being treated with an ESA:
Dose based on pre-treatment hemoglobin level
- Initial: Oral: 300 mg once daily.
- Adjust dose in increments of 150 mg to achieve or maintain hemoglobin levels of 10 g/dL to 11 g/dL. Doses may range from 150 mg to a maximum of 600 mg.

Member switching from an ESA:
- Starting dose: 300 mg by mouth once daily
- Owing to the gradual rise in hemoglobin (Hb) with vadadustat, RBC transfusions or ESA treatment may be considered during transition phase if Hb values fall to <9 g/dL or Hb response is considered unacceptable
- Patients receiving RBC transfusions should continue vadadustat during the transfusion period
- Pause vadadustat for those patients receiving temporary ESA rescue treatment and resume when Hb levels ≥10 g/dL

- Depending on ESA used for rescue, extend pause in vadadustat treatment to
  - 2 days after last dose of epoetin
  - 7 days after last dose of darbepoetin alfa
  - 14 days (about 2 weeks) after last dose of methoxy polyethylene glycol-epoetin beta
- Following ESA rescue, resume vadadustat at previous dose or with a dose that is 150 mg greater than the prior dose, with subsequent titration

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:

Vadadustat is the second approved oral treatment for anemia in CKD in adults on dialysis for at least 3 months. It is a hypoxia-inducible factor prolyl hydroxylase inhibitor, a class of compounds that stimulate endogenous erythropoietin production.

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.

The approval of Vafseo is based on efficacy and safety results from two phase III global, multicenter, randomized, double-blind active-controlled, noninferiority, open-label, 52-week INNO2VATE-1 (NCT02865850) and INNO2VATE-2 (NCT02892149) trials, along with post-marketing safety data from patients in Japan. These studies enrolled patients with DD-CKD, initiated dialysis ≤ 16-weeks, ESA naïve, had limited prior ESA use or were maintained on ESAs for INNO2VATE-1, and for INNO2VATE-2 patients on dialysis for ≥ 12-weeks who converted from prior ESA therapy.

A total of 3923 patients were randomly assigned in a 1:1 ratio to receive vadadustat or darbepoetin alfa - 369 in the incident DD-CKD trial and 3554 in the prevalent DD-CKD trial. In the pooled analysis, a first MACE occurred in 355 patients (18.2%) in the vadadustat group and in 377 patients (19.3%) in the darbepoetin alfa group (hazard ratio, 0.96; 95% confidence interval [CI], 0.83 to 1.11). The mean differences between the groups in the change in hemoglobin concentration were −0.31 g per deciliter (95% CI, −0.53 to −0.10) at weeks 24 to 36 and −0.07 g per deciliter (95% CI, −0.34 to 0.19) at weeks 40 to 52 in the incident DD-CKD trial and −0.17 g per deciliter (95% CI, −0.23 to −0.10) and −0.18 g per deciliter (95% CI, −0.25 to −0.12), respectively, in the prevalent DD-CKD trial. The incidence of serious adverse events in the vadadustat group was 49.7% in the incident DD-CKD trial and 55.0% in the prevalent DD-CKD trial, and the incidences in the darbepoetin alfa group were 56.5% and 58.3%, respectively.

Among patients with anemia and CKD who were undergoing dialysis, vadadustat was noninferior to darbepoetin alfa with respect to cardiovascular safety and correction and maintenance of hemoglobin concentrations.

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:

All other uses of Vafseo (vadadustat) are considered experimental/investigational and therefore, will follow Molina's Off- Label policy. Contraindications to Vafseo (vadadustat) include: known hypersensitivity to Vafseo or any of its components, and uncontrolled hypertension.

OTHER SPECIAL CONSIDERATIONS:

Vafseo (vadadustat) has a BLACK BOX WARNING for increased risk of death, myocardial infarction, stroke, venous thromboembolism, and thrombosis of vascular access. Vafseo increases the risk of thrombotic vascular events, including major adverse cardiovascular events (MACE). Targeting a

hemoglobin level greater than 11 g/dL is expected to further increase the risk of death and arterial and 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 Vafseo, or dosing strategy that does not increase these risks. Use the lowest dose of Vafseo sufficient to reduce the need for red blood cell transfusions.

Patients with CKD taking Vafseo (vadadustat) need to be monitored for new onset seizures, premonitory symptoms, or change in seizure frequency. Additionally, signs and symptoms of gastric or esophageal erosions and gastrointestinal bleeding need to be monitored in patients with history of GI erosions or peptic ulcer disease, use of concomitant medications that increase the risk of gastrointestinal erosion, and current tobacco smokers and alcohol drinkers.

CODING/BILLING INFORMATION

CODING DISCLAIMER. *Codes listed in this policy are for reference purposes only and may not be all-inclusive or applicable for every state or line of business. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement. Listing of a service or device code in this policy does not guarantee coverage. Coverage is determined by the benefit document. Molina adheres to Current Procedural Terminology (CPT®), a registered trademark of the American Medical Association (AMA). All CPT codes and descriptions are copyrighted by the AMA; this information is included for informational purposes only. Providers and facilities are expected to utilize industry-standard coding practices for all submissions. Molina has the right to reject/deny the claim and recover claim payment(s) if it is determined it is not billed appropriately or not a covered benefit. Molina reserves the right to revise this policy as needed.*

HCPCS CODE	DESCRIPTION
NA	

AVAILABLE DOSAGE FORMS:
Vafseo TABS 150MG
Vafseo TABS 300MG
Vafseo TABS 450MG

REFERENCES

1. Vafseo (vadadustat) tablets, for oral use [prescribing information]. Cambridge, MA: Akebia Therapeutics, Inc.; March 2024.
2. Eckardt, K.-U., Agarwal, R., Aswad, A., Awad, A., Block, G. A., Bacci, M. R., … Sarnak, M. J. (2021). Safety and Efficacy of Vadadustat for Anemia in Patients Undergoing Dialysis. New England Journal of Medicine, 384(17), 1601–1612. https://doi.org/10.1056/nejmoa2025956
3. Akebia Receives FDA Approval of Vafseo® (vadadustat) Tablets for the Treatment of Anemia due to Chronic Kidney Disease in Adult Patients on Dialysis | Akebia Therapeutics. (2024, March 27). Retrieved August 27, 2024, from Akebia Therapeutics website: https://ir.akebia.com/news-releases/news-release-details/akebia-receives-fda-approval-vafseor-vadadustat-tablets
4. 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

SUMMARY OF REVIEW/REVISIONS	DATE
NEW CRITERIA CREATION	Q4 2024