In adults with anemia due to chronic kidney disease (CKD) who have been on dialysis for at least 3 months

Vafseo is a HIF-PHI that stimulates endogenous EPO production[1-3]

Discover once-daily oral Vafseo® (vadadustat)

EPO=erythropoietin; HIF-PHI=hypoxia-inducible factor prolyl hydroxylase inhibitor.

INDICATION

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

- VAFSEO has not been shown to improve quality of life, fatigue, or patient well-being.
- VAFSEO 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.

IMPORTANT SAFETY INFORMATION about VAFSEO (vadadustat) tablets

WARNING: 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.

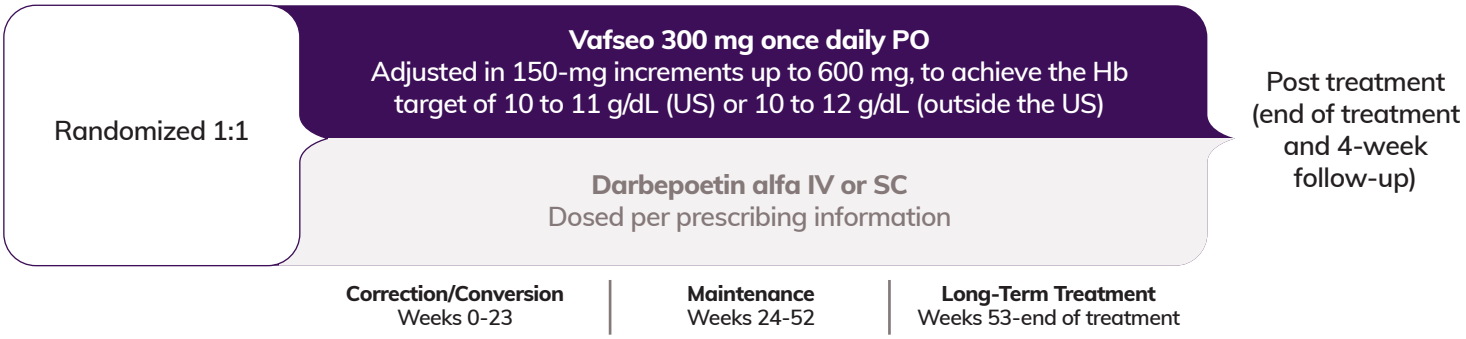
Please see additional Important Safety Information throughout. Please click here for the Full Prescribing Information, including BOXED WARNING and Medication Guide or visit VafseoHCP.com.

Vafseo® (vadadustat) Tablets

Vafseo® (vadadustat) was studied in ~2,000 patients on dialysis with anemia due to CKD[1,2,4]

Trial Design

The efficacy and safety of Vafseo were evaluated in 2 global, phase 3, multi-center, randomized, active-controlled, non-inferiority, open-label trials (N=3923), $INNO_2VATE$-1 and $INNO_2VATE$-2.



Limitations:

Residual kidney function was not measured but results were uniform across all dialysis durations in all trial patients with DD-CKD.

Key clinical trial endpoints:

- **Efficacy:** Difference in mean change of Hb levels from baseline to primary (Weeks 24 to 36) and secondary (Weeks 40 to 52) evaluation periods, using the pre-specified, non-inferiority margin of -0.75 g/dL

- **Cardiovascular outcomes:** After 52 weeks, patients continued on study medication to assess long-term safety until the event-driven MACE* endpoints were reached. Time to first occurence of MACE was assessed in a pooled analysis of both trials, using the pre-specified, non-inferiority margin of 1.25

CKD=chronic kidney disease; DD-CKD=dialysis-dependent chronic kidney disease; ESA=erythropoiesis-stimulating agent; IV=intravenous; MACE=major adverse cardiovascular event; PO=by mouth; SC=subcutaneous.

*MACE is defined as a composite of death from any cause, a nonfatal myocardial infarction, or a nonfatal stroke.

IMPORTANT SAFETY INFORMATION (cont.)

CONTRAINDICATIONS

- Known hypersensitivity to VAFSEO or any of its components
- Uncontrolled hypertension

WARNINGS AND PRECAUTIONS

- **Increased Risk of Death, Myocardial Infarction (MI), Stroke, Venous Thromboembolism, and Thrombosis of Vascular Access**

  A rise in hemoglobin (Hb) levels greater than 1 g/dL over 2 weeks can increase these risks. Avoid in patients with a history of MI, cerebrovascular event, or acute coronary syndrome within the 3 months prior to starting VAFSEO. Targeting a Hb level of greater than 11 g/dL is expected to further increase the risk of death and arterial and venous thrombotic events. Use the lowest effective dose to reduce the need for red blood cell (RBC) transfusions. Adhere to dosing and Hb monitoring recommendations to avoid excessive erythropoiesis.

Please see additional Important Safety Information throughout. Please click here for the Full Prescribing Information, including BOXED WARNING and Medication Guide or visit VafseoHCP.com.

Patients in the Vafseo® (vadadustat) pivotal trials[1,2,4]

Patient Population	Incident Dialysis Trial ($INNO_2VATE$-1)		Prevalent Dialysis Trial ($INNO_2VATE$-2)	
	Vafseo (n=181)	**Darbepoetin alfa** (n=188)	**Vafseo** (n=1777)	**Darbepoetin alfa** (n=1777)
CKD Status	Incident dialysis patient for ≤16 weeks		Maintenance dialysis patient for ≥12 weeks	
ESA Status	ESA-naive, limited prior ESA use, or maintained on ESAs		Maintained on ESAs	
Baseline Hb Values	8 to 11 g/dL (US and outside the US)		8 to 11 g/dL (US) 9 to 12 g/dL (outside the US)	
Iron Status	Serum ferritin ≥100 ng/mL Transferrin saturation ≥20%		Serum ferritin ≥100 ng/mL Transferrin saturation ≥20%	

- **Key exclusion criteria:** Patients with anemia due to non-CKD causes, uncontrolled hypertension, or a recent cardiovascular event, were excluded from the trials

IMPORTANT SAFETY INFORMATION (cont.)

WARNINGS AND PRECAUTIONS (cont.)

- **Hepatotoxicity**

  Hepatocellular injury attributed to VAFSEO was reported in less than 1% of patients, including one severe case with jaundice. Elevated serum ALT, AST, and bilirubin levels were observed in 1.8%, 1.8%, and 0.3% of CKD patients treated with VAFSEO, respectively. Measure ALT, AST, and bilirubin before treatment and monthly for the first 6 months, then as clinically indicated. Discontinue VAFSEO if ALT or AST is persistently elevated or accompanied by elevated bilirubin. Not recommended in patients with cirrhosis or active, acute liver disease.

- **Hypertension**

  Worsening of hypertension was reported in 14% of VAFSEO and 17% of darbepoetin alfa patients. Serious worsening of hypertension was reported in 2.7% of VAFSEO and 3% of darbepoetin alfa patients. Cases of hypertensive crisis, including hypertensive encephalopathy and seizures, have also been reported in patients receiving VAFSEO. Monitor blood pressure. Adjust anti-hypertensive therapy as needed.

Please see additional Important Safety Information throughout. Please click here for the Full Prescribing Information, including BOXED WARNING and Medication Guide or visit VafseoHCP.com.

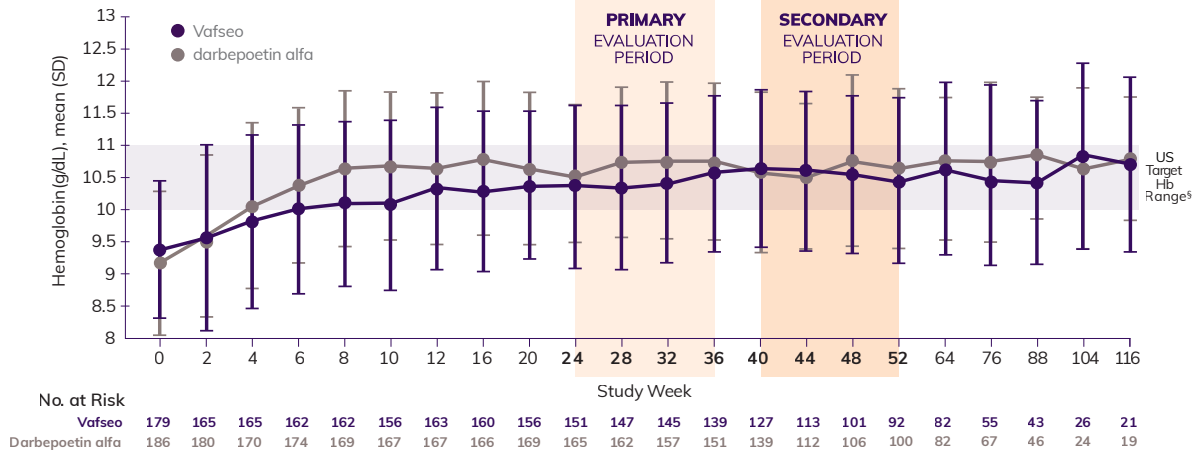
Adult patients who took Vafseo® (vadadustat) achieved and sustained target Hb levels[1,2,4]

Non-inferiority of Vafseo compared to an ESA† was established at weeks 24-36 and weeks 40-52 because the lower bound of the 95% CI for the treatment difference in mean change in Hb from baseline was less than the pre-specified, non-inferiority margin of -0.75 g/dL.

Trials were designed where all DD-CKD patients treated with Vafseo received the same starting dose of 300 mg orally, once daily, regardless of prior ESA dose.

	Incident Dialysis Trial[a] (INNO$_2$VATE-1)*†	
Hemoglobin (g/dL)	**Vafseo** (n=181)	**Darbepoetin alfa** (n=188)
Baseline mean (SD)	9.4 (1.1)	9.2 (1.1)
Weeks 24 to 36 Mean Hb (SD)	10.4 (1.1)	10.6 (0.9)
Treatment difference‡ [95% CI] Vafseo - darbepoetin alfa	**-0.3 [-0.5, -0.1]**	
Weeks 40 to 52 Mean Hb (SD)	10.5 (1.2)	10.6 (1.1)
Treatment difference‡ [95% CI] Vafseo - darbepoetin alfa	**-0.1 [-0.3, 0.2]**	
Non-inferiority margin to determine efficacy	**-0.75 g/dL**	

Mean Hb Levels Over Time[2,5*]



Data outside of the primary and secondary evaluation periods are descriptive.

*Vafseo is approved for adults with anemia due to CKD who have been on dialysis for at least 3 months.

†Darbepoetin alfa was the control used in both clinical trials and therefore non-inferiority to other ESAs cannot be concluded. A protocol-specified algorithm was used for both treatment groups to achieve and maintain Hb levels to target range.[2,5]

‡Treatment difference is based on the LS mean change from baseline. The estimated treatment difference (Vafseo – darbepoetin alfa) is obtained from an analysis of covariance (ANCOVA) model (treatment group, baseline Hb level, stratification factors [region and NYHA-CHF] as predictor variables) with multiple imputations. Hemoglobin levels were monitored throughout the study per protocol.[1,2]

§Target Hb ranges were 10 to 11 g/dL in the US and 10 to 12 g/dL outside the US. Vertical bars denote mean ± SD.[2]

IMPORTANT SAFETY INFORMATION (cont.)

WARNINGS AND PRECAUTIONS (cont.)

- **Seizures**

  Seizures occurred in 1.6% of VAFSEO and 1.6% of darbepoetin alfa patients. Monitor for new-onset seizures, premonitory symptoms, or change in seizure frequency.

Please see additional Important Safety Information throughout. Please click here for the Full Prescribing Information, including BOXED WARNING and Medication Guide or visit VafseoHCP.com.

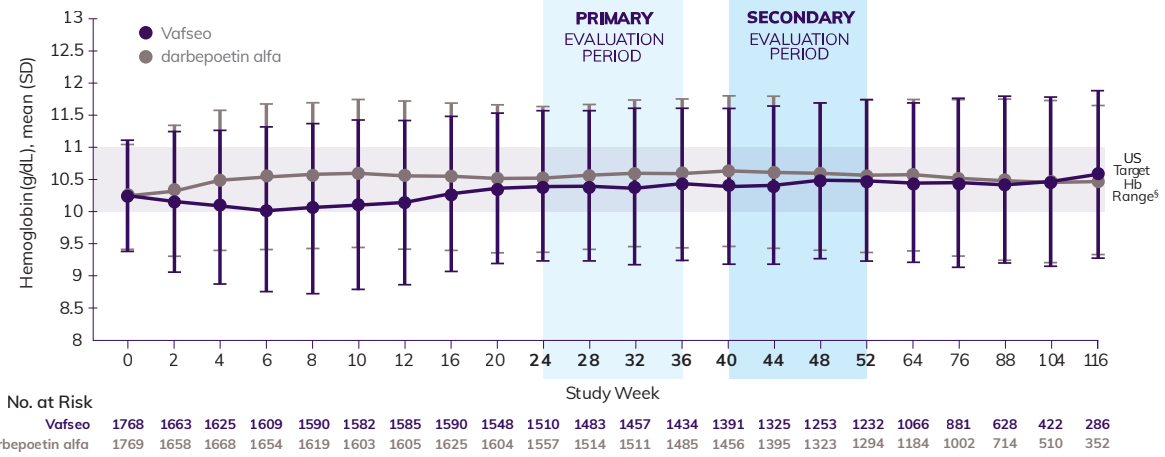
Adult patients who took Vafseo® (vadadustat) achieved and sustained target Hb levels[1,2,4]

Non-inferiority of Vafseo compared to an ESA† was established at weeks 24-36 and weeks 40-52 because the lower bound of the 95% CI for the treatment difference in mean change in Hb from baseline was less than the pre-specified, non-inferiority margin of -0.75 g/dL.

Trials were designed where all DD-CKD patients treated with Vafseo received the same starting dose of 300 mg orally, once daily, regardless of prior ESA dose.

	Prevalent Dialysis Trial (INNO$_2$VATE-2)	
Hemoglobin (g/dL)	**Vafseo** (n=1777)	**Darbepoetin alfa** (n=1777)
Baseline mean (SD)	10.3 (0.9)	10.2 (0.8)
Weeks 24 to 36 Mean Hb (SD)	10.4 (1.0)	10.5 (1.0)
Treatment difference‡ [95% CI] Vafseo - darbepoetin alfa	-0.2 [-0.2, -0.1]	
Weeks 40 to 52 Mean Hb (SD)	10.4 (1.0)	10.6 (1.0)
Treatment difference‡ [95% CI] Vafseo - darbepoetin alfa	-0.2 [-0.3, -0.1]	
Non-inferiority margin to determine efficacy	-0.75 g/dL	

Mean Hb Levels Over Time[2,5]



Data outside of the primary and secondary evaluation periods are descriptive.

CI=confidence interval; DD-CKD=dialysis-dependent chronic kidney disease; ESA=erythropoiesis-stimulating agent; LS=least squares; NYHA-CHF=New York Heart Association-Congestive Heart Failure; SD=standard deviation.

†Darbepoetin alfa was the control used in both clinical trials and therefore non-inferiority to other ESAs cannot be concluded. A protocol-specified algorithm was used for both treatment groups to achieve and maintain Hb levels to target range.[2,5]

‡Treatment difference is based on the LS mean change from baseline. The estimated treatment difference (Vafseo – darbepoetin alfa) is obtained from an analysis of covariance (ANCOVA) model (treatment group, baseline Hb level, stratification factors [region and NYHA-CHF] as predictor variables) with multiple imputations. Hemoglobin levels were monitored throughout the study per protocol.[1,2]

§Target Hb ranges were 10 to 11 g/dL in the US and 10 to 12 g/dL outside the US. Vertical bars denote mean ± SD.[2]

IMPORTANT SAFETY INFORMATION (cont.)

WARNINGS AND PRECAUTIONS (cont.)

- **Gastrointestinal (GI) Erosion**

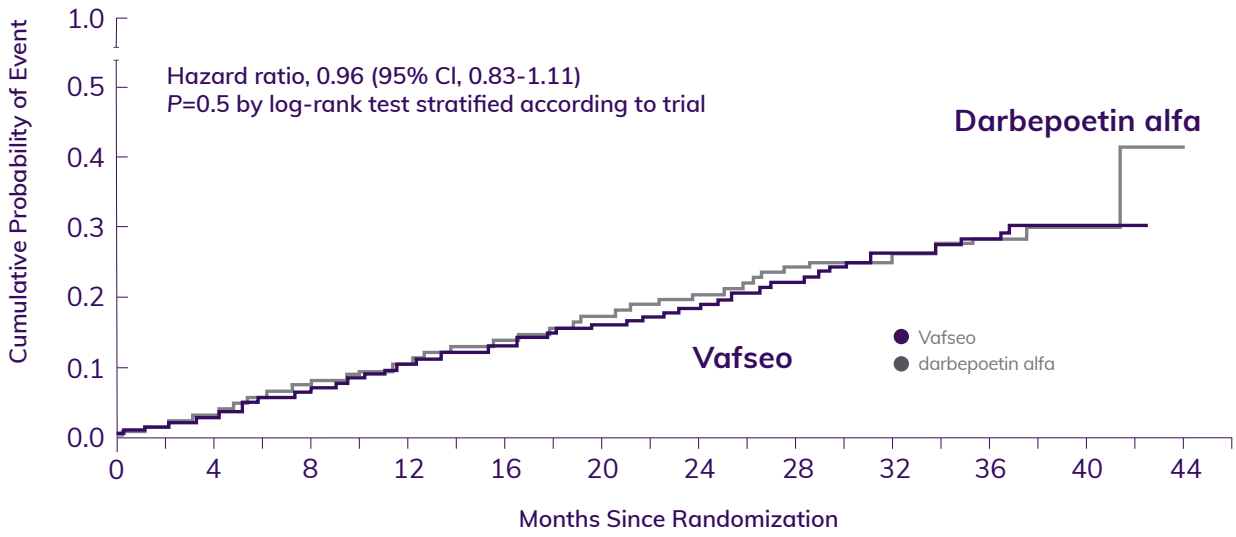
  Gastric or esophageal erosions occurred in 6.4% of VAFSEO and 5.3% of darbepoetin alfa patients.

Please see additional Important Safety Information throughout. Please click here for the Full Prescribing Information, including BOXED WARNING and Medication Guide or visit VafseoHCP.com.

Vafseo® (vadadustat) was similar to an ESA* in time to first occurrence of MACE[1,2†]

Non-inferiority of Vafseo was established because the upper-bound of the 95% CI for the MACE hazard ratio was less than the pre-specified non-inferiority margin of 1.25.

Time to First MACE in the Pooled Safety Population of Both Dialysis Trials



No. at Risk												
Vafseo	**1947**	**1881**	**1801**	**1615**	**1372**	**1040**	**711**	**491**	**262**	**89**	**6**	**0**
Darbepoetin alfa	1955	1893	1807	1628	1393	1053	718	491	265	94	13	1

CI=confidence interval; ESA=erythropoiesis-stimulating agent; MACE=major adverse cardiac event.

*Darbepoetin alfa was the control used in both clinical trials and therefore non-inferiority to other ESAs cannot be concluded.
†MACE was defined as all-cause mortality, non-fatal myocardial infarction, and non-fatal stroke.

IMPORTANT SAFETY INFORMATION (cont.)

WARNINGS AND PRECAUTIONS (cont.)

- **Gastrointestinal (GI) Erosion (cont.)**
  Serious GI erosions, including GI bleeding and the need for RBC transfusions, were reported in 3.4% of VAFSEO and 3.3% of darbepoetin alfa patients. Consider this risk in patients at increased risk of GI erosion. Advise patients about signs of erosions and GI bleeding and urge them to seek prompt medical care if present.
- **Serious Adverse Reactions in Patients with Anemia Due to CKD and Not on Dialysis**
  The safety of VAFSEO has not been established for the treatment of anemia due to CKD in adults not on dialysis and its use is not recommended in this setting. In large clinical trials in adults with anemia of CKD who were not on dialysis, an increased risk of mortality, stroke, MI, serious acute kidney injury, serious hepatic injury, and serious GI erosions was observed in patients treated with VAFSEO compared to darbepoetin alfa.

Please see additional Important Safety Information throughout. Please click here for the Full Prescribing Information, including BOXED WARNING and Medication Guide or visit VafseoHCP.com.

Vafseo® (vadadustat) has a well-studied safety profile[1,2]

Adverse Reactions (≥5%) in Patients with DD-CKD During INNO$_2$VATE-1 and INNO$_2$VATE-2

Adverse Reactions	Vafseo N=1947 (%)	Darbepoetin alfa N=1955 (%)
Hypertension‡	14	17
Diarrhea‡	13	10
Headache‡	9	8
Nausea‡	8	8
Fatigue‡	8	5
Abdominal pain‡	7	7
Vomiting‡	7	7
GI erosion‡	6	5
Dizziness‡	6	5
Dyspnea‡	6	7
AV fistual thrombosis	6	5
Dialysis-related complication	5	7

- Permanent treatment discontinuation due to an adverse reaction was reported in 4.9% of patients treated with Vafseo and 1.1% patients treated with darbepoetin alfa. Gastrointestinal symptoms (nausea, vomiting, and diarrhea) resulted in permanent treatment discontinuation in 1.8% of patients treated with Vafseo

- Adjudicated fatal and non-fatal thrombotic vascular events were observed in 9.0 per 100 PY of patients in the pooled Vafseo arm and in 8.7 per 100 PY of patients in the pooled darbepoetin alfa

AV=arteriovenous; DD-CKD=dialysis-dependent chronic kidney disease; ESA=erythropoiesis-stimulating agent; GI=gastrointestinal; MACE=major adverse cardiovascular event; PY=person years.

‡Grouped terms. Hypertension includes hypertensive crisis, pre-eclampsia, and hypertensive encephalopathy. Headache includes occipital neuralgia. Fatigue includes asthenia, lethargy, and malaise. Vomiting includes hematemesis. GI erosion includes duodenal ulcers and perforation, GI ulcers and perforation, esophageal ulcers and perforation, and unspecified site or hematemesis, GI hemorrhage, helicobacter duodenitis and gastritis, melaena, and gastric hemorrhage. Dizziness includes labyrinthitis, vertigo, vestibular neuronitis, and presyncope. Dyspnea includes orthopnea and respiratory distress.

IMPORTANT SAFETY INFORMATION (cont.)

WARNINGS AND PRECAUTIONS (cont.)

- **Malignancy**
  VAFSEO has not been studied and is not recommended in patients with active malignancies. Malignancies were observed in 2.2% of VAFSEO and 3.0% of darbepoetin alfa patients. No evidence of increased carcinogenicity was observed in animal studies.

Please see additional Important Safety Information throughout. Please click here for the Full Prescribing Information, including BOXED WARNING and Medication Guide or visit VafseoHCP.com.

Vafseo® (vadadustat) is available as a convenient, once-daily oral tablet[1]

The recommended starting dose is 300 mg once-daily

Assess and Monitor

- Before initiating Vafseo, correct and rule out other causes of anemia, check iron levels, measure baseline Hb, and measure liver function
- Measure Hb levels every 2 weeks until stable, then monitor at least monthly after dose initiation or adjustment
- Conduct liver function testing monthly for the first 6 months, then monitor as clinically indicated
- Evaluate iron status during treatment to assess the need for supplemental iron

Dose Adjustments

- Adjust in increments of 150 mg (between 150 mg and max. 600 mg) to achieve or maintain Hb levels within 10-11 g/dL
- Do not increase the dose more than once every 4 weeks; dose decreases can occur more frequently
- Consider the patient's Hb variability, Hb rate of rise and decline, and responsiveness to Vafseo when adjusting the dose. A single Hb excursion may not require a dosing change

Dose Interruptions and Discontinuations

- Vafseo should be interrupted for Hb exceeding 11 g/dL or temporary ESA rescue. In cases of rapid Hb rise, Vafseo should be interrupted or the dose reduced
- Vafseo should be discontinued if no clinically meaningful increase in Hb is achieved after 24 weeks. Vafseo can be restarted after treating alternative explanations for inadequate response

Refer to Section 2 of the Vafseo Full Prescribing Information for additional information.

Important Dosing Information

- Individualize dosing and use the lowest dose of Vafseo sufficient to reduce the need for red blood cell transfusions. Do not target a hemoglobin level higher than 11 g/dL
- Vafseo can be administered without regard to the timing or type of dialysis
- Vafseo can be taken with or without food
- Vafseo should be swallowed whole. Tablets should not be cut, crushed, or chewed

Oral Iron & Phosphate Binders

- Administer Vafseo at least 1 hour before oral iron supplements, products containing iron, or iron-containing phosphate binders
- Administer Vafseo at least 1 hour before or 2 hours after non-iron-containing phosphate binders

Hb=hemoglobin.

IMPORTANT SAFETY INFORMATION (cont.)

ADVERSE REACTIONS

- The most common adverse reactions (occurring at ≥ 10%) were hypertension and diarrhea.

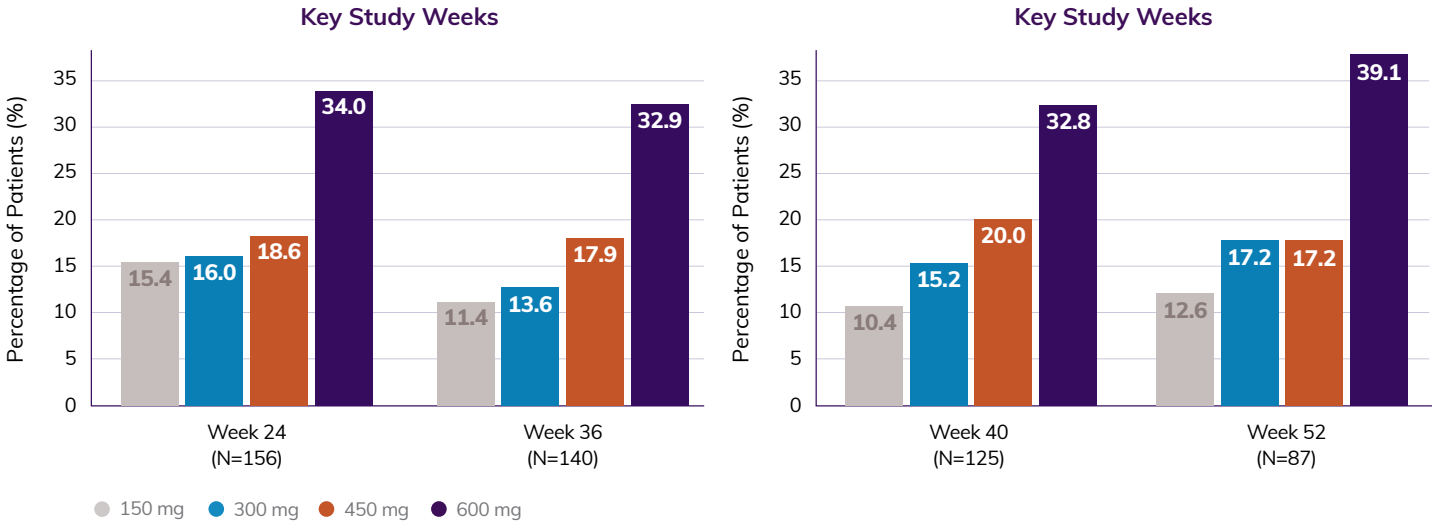
DRUG INTERACTIONS

- **Iron supplements and iron-containing phosphate binders:** Administer VAFSEO at least 1 hour before products containing iron.
- **Non-iron-containing phosphate binders:** Administer VAFSEO at least 1 hour before or 2 hours after non-iron-containing phosphate binders.
- **BCRP substrates:** Monitor for signs of substrate adverse reactions and consider dose reduction.
- **Statins:** Monitor for statin-related adverse reactions. Limit the daily dose of simvastatin to 20 mg and rosuvastatin to 5 mg.

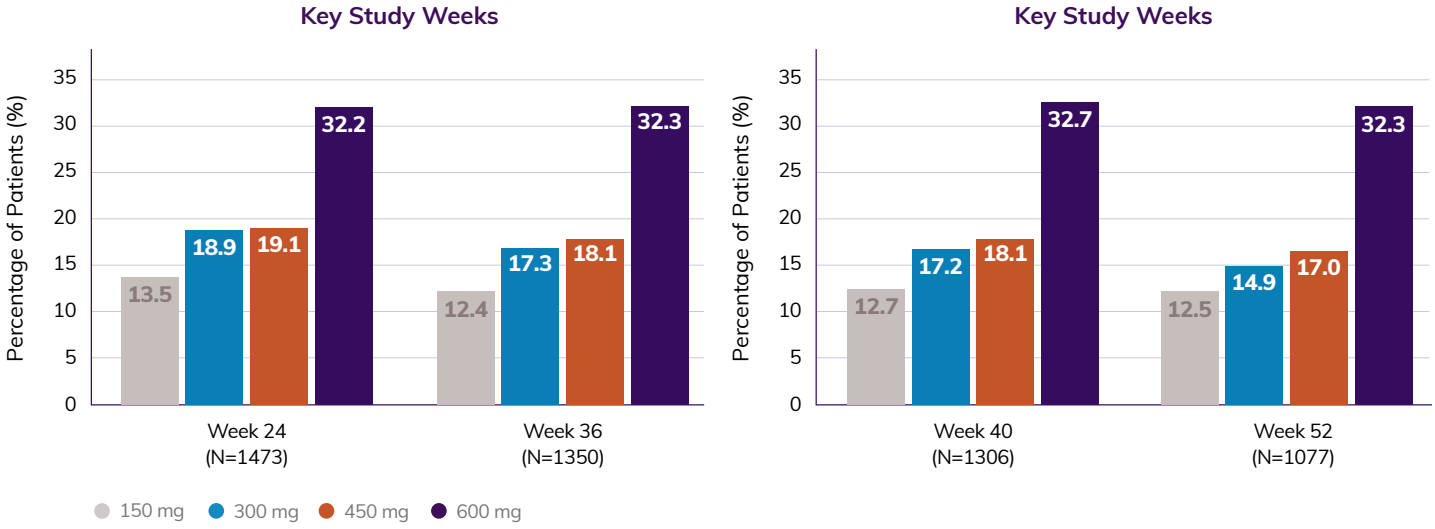
Please see additional Important Safety Information throughout. Please click here for the Full Prescribing Information, including BOXED WARNING and Medication Guide or visit VafseoHCP.com.

Vafseo® (vadadustat) dosing in pivotal trials[1,4,5]

Percent of Subjects by Vafseo Dose Level: Incident Dialysis Trial (INNO$_2$VATE-1)*



Percent of Subjects by Vafseo Dose Level: Prevalent Dialysis Trial (INNO$_2$VATE-2)*



Data presented are the most common administered dose received during that study week. Data are observational and doses may have been increased or decreased per protocol. Dose adjustment protocol in clinical trials is reflective of the Vafseo US Prescribing Information (USPI).

*Omits % of patients on 0 mg.

IMPORTANT SAFETY INFORMATION (cont.)

USE IN SPECIFIC POPULATIONS

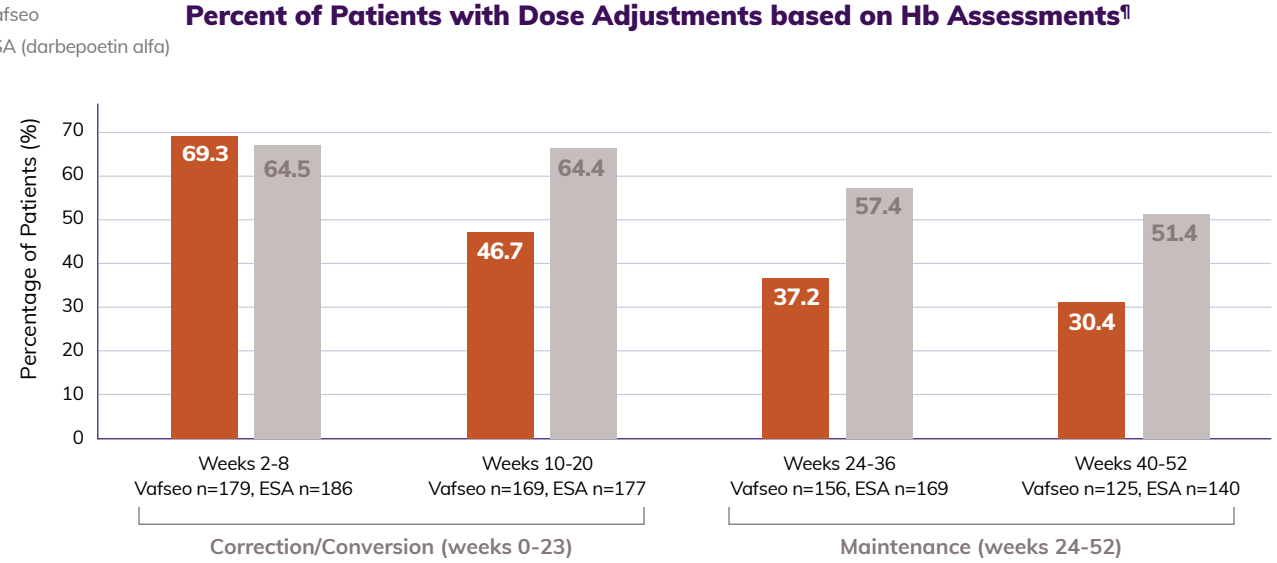
- Pregnancy: May cause fetal harm.
- Lactation: Breastfeeding not recommended until two days after the final dose.
- Hepatic Impairment: Not recommended in patients with cirrhosis or active, acute liver disease.

Please see additional Important Safety Information throughout. Please click here for the Full Prescribing Information, including BOXED WARNING and Medication Guide or visit VafseoHCP.com.

Dose adjustments based on Hb assessments[5*†]

INCIDENT DIALYSIS TRIAL (INNO$_2$VATE-1): Other efficacy endpoints included dose adjustments[4]

Percent of Patients with Dose Adjustments based on Hb Assessments[¶]



Dose Modifications for Other Reasons

Study Parameter	Primary Evaluation Period Weeks 24-36		Secondary Evaluation Period Weeks 40-52	
	Vafseo N=179 n(%)	**darbepoetin alfa** N=186 n(%)	**Vafseo** N=179 n(%)	**darbepoetin alfa** N=186 n(%)
Number of subjects not discontinuing study treatment permanently	156	169	125	140
Reasons for dose modifications‡				
Dosing interrupted due to elevated Hb	29 (18.6)	52 (30.8)	23 (18.4)	28 (20.0)
Dose decreased due to AE	0	0	0	0
Dose interrupted due to AE	6 (3.8)	5 (3.0)	2 (1.6)	4 (2.9)
Dose modifications for ESA rescue[6§]	23 (14.7)	19 (11.2)	19 (15.2)	13 (9.3)
Dosing restarted	34 (21.8)	48 (28.4)	37 (29.6)	34 (24.3)

Presented data are a descriptive summary using observed data. Data were not corrected for multiplicity. All analyses should be interpreted with caution.

AE=adverse event; ESA=erythropoiesis-stimulating agent; Hb=hemoglobin.

*The darbepoetin alfa dose adjustment algorithm followed the US Prescribing Information (USPI) for US sites and the Summary of Product Characteristics for non-US sites. Vafseo dose adjustments were guided by a protocol-specific dose adjustment algorithm, reflected in the Vafseo USPI.[5]

†Vafseo and darbepoetin alfa dose increases, decreases, or interruptions to maintain Hb within geography-specific target range were determined by HemoCue, local laboratory, or central laboratory. From Weeks 0-12, Hb was monitored every 2 weeks. From Weeks 12 to 52, Hb was monitored every 4 weeks unless more frequent monitoring was clinically indicated or warranted based on dosing changes.[5]

‡Each subject may be counted into multiple categories. Percentage of dose modifications for other reasons in the primary evaluation period were 2 (1.3%) for Vafseo and 5 (3.0%) for darbepoetin alfa; and in the secondary evaluation period were 1 (0.8%) for Vafseo and 2 (1.4%) for darbepoetin alfa.[5]

§Starting at week 6, patients in both treatment groups could receive ESAs as "rescue" therapy if they experienced worsening symptoms of anemia of CKD with hemoglobin concentration <9.5 g/dL. In the darbepoetin alfa group, ESA was considered to be a rescue medication if the dose was at least double that of the previous dose. Vadadustat was interrupted for patients who received ESA rescue; darbepoetin alfa was interrupted if another ESA was used for rescue.[2]

¶Dose adjustments defined as a dose increase or a dose decrease.

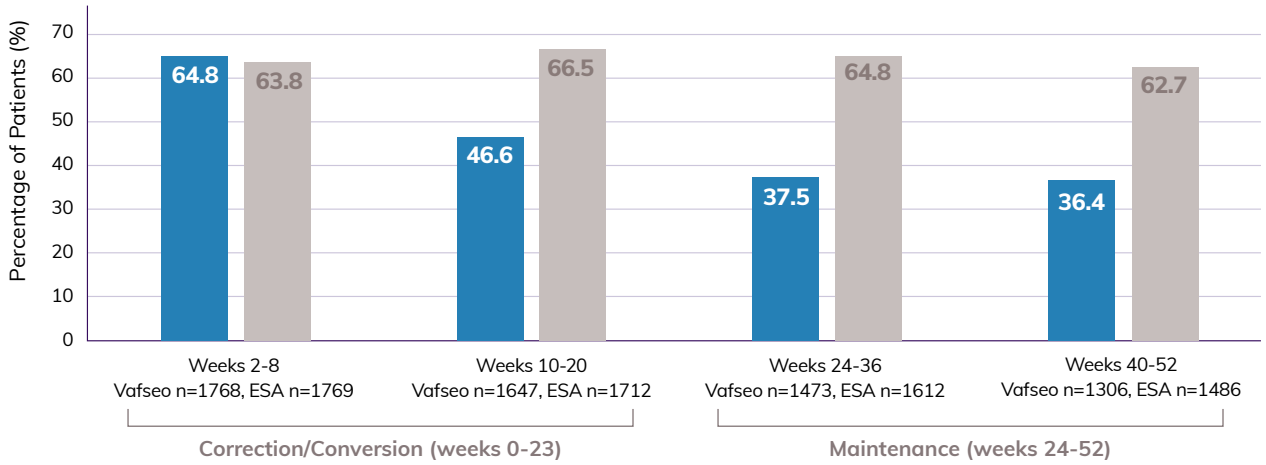
Please see Important Safety Information throughout. Please click here for the Full Prescribing Information, including BOXED WARNING and Medication Guide or visit VafseoHCP.com.

Dose adjustments based on Hb assessments[5*†]

PREVALENT DIALYSIS TRIAL (INNO$_2$VATE-2): Other efficacy endpoints included dose adjustments[4]

Vafseo
ESA (darbepoetin alfa)

Percent of Patients with Dose Adjustments based on Hb Assessments[¶]



Dose Modifications for Other Reasons

Study Parameter	Primary Evaluation Period Weeks 24-36		Secondary Evaluation Period Weeks 40-52	
	Vafseo N=1768 n(%)	**darbepoetin alfa** N=1769 n(%)	**Vafseo** N=1768 n(%)	**darbepoetin alfa** N=1769 n(%)
Number of subjects not discontinuing study treatment permanently	1473	1612	1306	1486
Reasons for dose modifications‡				
Dosing interrupted due to elevated Hb	308 (20.9)	507 (31.5)	285 (21.8)	488 (32.8)
Dose decreased due to AE	3 (0.2)	0	2 (0.2)	0
Dose interrupted due to AE	59 (4.0)	44 (2.7)	48 (3.7)	41 (2.8)
Dose modifications for ESA rescue[6§]	253 (17.2)	301 (18.7)	273 (20.9)	260 (17.5)
Dosing restarted	463 (31.4)	543 (33.7)	443 (33.9)	594 (40.0)

Presented data are a descriptive summary using observed data. Data were not corrected for multiplicity. All analyses should be interpreted with caution.

AE=adverse event; ESA=erythropoiesis-stimulating agent; Hb=hemoglobin.

*The darbepoetin alfa dose adjustment algorithm followed the US Prescribing Information (USPI) for US sites and the Summary of Product Characteristics for non-US sites. Vafseo dose adjustments were guided by a protocol-specific dose adjustment algorithm, reflected in the Vafseo USPI.[5]

†Vafseo and darbepoetin alfa dose increases, decreases, or interruptions to maintain Hb within geography-specific target range were determined by HemoCue, local laboratory, or central laboratory. From Weeks 0-12, Hb was monitored every 2 weeks. From Weeks 12 to 52, Hb was monitored every 4 weeks unless more frequent monitoring was clinically indicated or warranted based on dosing changes.[5]

‡Each subject may be counted into multiple categories. Percentage of dose modifications for other reasons in the primary evaluation period were 37 (2.5%) for Vafseo and 66 (4.1%) for darbepoetin alfa; and in the secondary evaluation period 36 (2.8%) for Vafseo and 82 (5.5%) for darbepoetin alfa.[5]

§Starting at week 6, patients in both treatment groups could receive ESAs as "rescue" therapy if they experienced worsening symptoms of anemia of CKD with hemoglobin concentration <9.5 g/dL. In the darbepoetin alfa group, ESA was considered to be a rescue medication if the dose was at least double that of the previous dose. Vadadustat was interrupted for patients who received ESA rescue; darbepoetin alfa was interrupted if another ESA was used for rescue.[2]

¶Dose adjustments defined as a dose increase or a dose decrease.

Please see Important Safety Information throughout. Please click here for the Full Prescribing Information, including BOXED WARNING and Medication Guide or visit VafseoHCP.com.

For adults with anemia due to CKD on dialysis for at least 3 months

Once-daily oral Vafseo® (vadadustat) is an innovative HIF-PHI that controls Hb levels[1-3]

- **Vafseo** was non-inferior to an ESA† in achieving and sustaining Hb levels in two clinical trials of patients with anemia due to CKD and on dialysis[1,2]
- **Vafseo** was similar to an ESA† in time to first occurrence of MACE[1,2]

Vafseo offers a different treatment option for patients.

CKD=chronic kidney disease; ESA=erythropoiesis-stimulating agent; Hb=hemoglobin; MACE=major adverse cardiovascular event.

†Darbepoetin alfa was the control used in both clinical trials and therefore non-inferiority to other ESAs cannot be concluded. A protocol-specified algorithm was used for both treatment groups to achieve and maintain Hb levels to target range.[2,5]

SELECT IMPORTANT SAFETY INFORMATION

VAFSEO has a BOXED WARNING for INCREASED RISK OF DEATH, MYOCARDIAL INFARCTION, STROKE, VENOUS THROMBOEMBOLISM, and THROMBOSIS OF VASCULAR ACCESS.

- VAFSEO is contraindicated in patients with hypersensitivity to VAFSEO or any of its components, and patients with uncontrolled hypertension.
- VAFSEO has warnings and precautions for Increased Risk of Death, Myocardial Infarction, Stroke, Venous Thromboembolism, and Thrombosis of Vascular Access; Hepatotoxicity; Hypertension; Seizures; Gastrointestinal Erosion; Serious Adverse Reactions in Patients with Anemia Due to CKD and Not on Dialysis; and Malignancy.
- The most common adverse reactions with VAFSEO were systemic hypertension and diarrhea.

Please note this information is not comprehensive, see additional Important Safety Information throughout and accompanying Full Prescribing Information, including BOXED WARNING and Medication Guide.

References: 1. Vafseo. Prescribing information. Akebia Therapeutics, Inc. **2.** Eckardt K-U, Agarwal R, Aswad A, et al. Safety and efficacy of vadadustat for anemia in patients undergoing dialysis. *N Engl Med*. 2021;384(17):1601-1612. **3.** Gupta N, Wish JB. Hypoxia-inducible factor prolyl hydroxylase inhibitors... *Am J Kidney Dis*. 2017;69(6):815-826. **4.** Eckardt KU, Agarwal R, Farag YM, 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 INNO$_2$VATE trials. *Nephrol Dial Transplant*. 2021;36(11):2039-2048. **5.** Akebia Therapeutics. Data on File. **6.** Eckardt K-U, Agarwal R, Aswad A, et al. Safety and efficacy of vadadustat for anemia in patients undergoing dialysis. [supplementary appendix]. *N Engl Med*. 2021;384(17):1601-1612. https://www.nejm.org/doi/suppl/10.1056/NEJMoa2025956/suppl_file/nejmoa2025956_appendix.pdf. Accessed December 18, 2024.

Akebia® THERAPEUTICS

Akebia Therapeutics®, Vafseo®, and their associated logos are registered trademarks of Akebia and/or its affiliates.
© 2025 Akebia Therapeutics, Inc. All rights reserved.
PP-VAF-US-0070 (v2.0) 06/25

Vafseo® (vadadustat) Tablets