Jesduvroq (daprodustat) Prior Authorization with Quantity Limit Program Summary

This program applies to FlexRx Closed, FlexRx Open, FocusRx, GenRx Closed, GenRx Open, Health Insurance Marketplace, and KeyRx formularies.

This is a FlexRx standard and GenRx standard prior authorization.

POLICY REVIEW CYCLE

Effective Date	Date of Origin
1/1/2024	10/1/2023

FDA APPROVED INDICATIONS AND DOSAGE

Agent(s)	FDA Indication(s)	Notes	Ref#
Jesduvroq (daprodustat) Tablets	• Treatment of anemia due to chronic kidney disease in adults who have been receiving dialysis for at least 4 months Limitations of Use • Not 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 • In patients not on dialysis		1

See package insert for FDA prescribing information: https://dailymed.nlm.nih.gov/dailymed/index.cfm

CLINICAL RATIONALE

Anemia in chronic kidney disease	Anemia is a common complication of chronic kidney disease (CKD) associated with adverse outcomes. Relative erythropoietin deficiency and disordered iron hemostasis, including absolute and functional iron deficiency, are major contributors to the anemia of CKD. For patients with chronic kidney disease with anemia Kidney Disease Improving Global Outcomes (KIDGO) recommend hemoglobin (Hb) concentration be measured when clinically indicated and at least every 3 months in patients with CKD Stage 5 on peritoneal dialysis and at least monthly in patients with CKD Stage 5 on hemodialysis for those patients not on an erythropoietin receptor agonist (ESA). For patients on dialysis of any kind and on ESA therapy Hb should be measured at least monthly. Anemia is diagnosed in adults and children > 15 years of age with CKD when the Hb concentration is < 13.0 g/dL (< 130 g/L) in males and < 12.0 g/dL (<120 g/L) in females.(2) Correction of iron deficiency with oral or intravenous iron supplementation can reduce the severity of anemia in patients with CKD. Untreated iron deficiency is an important cause of hyporesponsiveness to ESA treatment. Iron supplementation is widely used in CKD patients to treat iron deficiency, prevent its development in ESA-treated patients, raise Hb levels in the presence or absence of ESA treatment, and reduce ESA doses in patients receiving ESA treatment. When prescribing iron therapy, balance the potential benefits of avoiding or minimizing blood transfusions, ESA therapy, and anemia related symptoms against the risks of harm in individual patients (e.g., anaphylactoid and other acute reactions, unknown long-term risks. For adult CKD patients with

	anemia KDIGO suggests a trial of intravenous (IV) iron in patients on dialysis regardless of ESA use.(2) For adult CKD Stage 5 dialysis patients KDIGO suggests that ESA therapy be used to avoid having the Hb concentration fall below 9.0 g/dL (90 g/L) by starting the ESA therapy when the hemoglobin is between 9.0-10.0 g/dL (90-100 g/dL). Individualization of therapy is reasonable as some patients may have improvements in quality of life at higher Hb concentration and ESA therapy may be started above 10.0 g/dL (100 g/dL).(2) Kidney Disease Outcomes Quality Initiative (KDOQI) agreed with the KDIGO recommendations on frequency of Hb concentration and generally agree with the ESA guidelines. Although KDOQI does agree that patients with anemia in CKD be treated with iron therapy, KDOQI does note that the KDIGO guidelines do not discriminate among the different IV iron preparations, instead referring only to iron dextran and nondextran iron. Although head-to-head comparisons of the safety and short-term side effects related to the administration of these different preparations do not exist, there is evidence that high-molecular-weight preparations (i.e., high-molecular-weight iron dextran), are associated with more adverse effects, specifically more acute reactions. Therefore, KDOQI recommends that high-molecular weight iron dextran be avoided.(3)
Efficacy(1)	Daprodustat is a reversible inhibitor of HIF-PH1, PH2 and PH3 (IC50 in the low nM range). This activity results in the stabilization and nuclear accumulation of HIF-1alfa and HIF2alfa transcription factors, leading to increased transcription of the HIF-responsive genes, including erythropoietin. The efficacy and safety of Jesduvroq were evaluated in a randomized, sponsor-blind, active-controlled, global, multicenter, event-driven clinical trial (ASCEND-D; NCT02879305) in adults with CKD on dialysis and receiving an ESA. 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 (HD) were randomized 1:1 to receive oral Jesduvroq or intravenous epoetin alfa while patients on peritoneal dialysis were randomize 1:1 to receive oral Jesduvroq or subcutaneous darbepoetin alfa. Key exclusion criteria included: • Ferritin less than or equal to 100 ng/mL (less than 100 mcg/L) • Transferrin saturation less than or equal to 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, New York Heart Association (NYHA) Class IV heart failure, and uncontrolled hypertension • Liver disease • History of malignancy within 2 years of screening • Current treatment of cancer and kidney cyst 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 (CI) 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 wither hemodialysis or peritoneal dialysis.
Safety(1)	• Jesduvroq contains a boxed warning containing the following: o Jesduvroq 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 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 Jesduvroq, or dosing strategy that does not increase these risks ○ Use lowest dose of Jesduvroq sufficient to reduce the need for red blood cell transfusions • Jesduvroq is contraindicated in: ○ Strong cytochrome P450 2C8 (CYP2C8) inhibitors such as gemfibrozil ○ Uncontrolled hypertension

REFERENCES

Number	Reference
1	Jesduvroq Prescribing Information. GlaxoSmithKline LLC. February 2023.
2	KDIGO Clinical Practice Guidelines for Anemia in Chronic Kidney Disease. Kidney Int Suppl 2012 Aug;2(4):279-335.
3	Kliger AS, Foley RN, Goldfarb DS, et al. KDOQI US Commentary on the 2012 KDIGO Clinical Practice Guideline for Anemia in CKD. Am J Kidney Dis. 2013;62(5):849-859.

POLICY AGENT SUMMARY PRIOR AUTHORIZATION

Target Brand Agent(s)	Target Generic Agent(s)	Strength	Targeted MSC	Available MSC	Final Age Limit	Preferred Status
Jesduvroq	daprodustat tab	1 MG ; 2 MG ; 4 MG ; 6 MG ; 8 MG	M ; N ; O ; Y	N		

POLICY AGENT SUMMARY QUANTITY LIMIT

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	QL Amount	Dose Form	Day Supply	Duration	Addtl QL Info	Allowed Exceptions	Targeted NDCs When Exclusions Exist
Jesduvroq	daprodustat tab	1 MG	30	Tablets	30	DAYS			
Jesduvroq	daprodustat tab	2 MG	30	Tablets	30	DAYS			
Jesduvroq	daprodustat tab	4 MG	30	Tablets	30	DAYS			
Jesduvroq	daprodustat tab	6 MG	60	Tablets	30	DAYS			
Jesduvroq	daprodustat tab	8 MG	90	Tablets	30	DAYS			

CLIENT SUMMARY – PRIOR AUTHORIZATION

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Jesduvroq	daprodustat tab	1 MG ; 2 MG ; 4 MG ; 6 MG ; 8 MG	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
			Marketplace/BasicRx ; KeyRx

CLIENT SUMMARY – QUANTITY LIMITS

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Jesduvroq	daprodustat tab	8 MG	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx
Jesduvroq	daprodustat tab	6 MG	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx
Jesduvroq	daprodustat tab	4 MG	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx
Jesduvroq	daprodustat tab	2 MG	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx
Jesduvroq	daprodustat tab	1 MG	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx

PRIOR AUTHORIZATION CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
	Initial Evaluation **Target Agent(s)** will be approved when ALL of the following are met: 1. ONE of the following: A. The requested agent is eligible for continuation of therapy AND ONE of the following: **Agents Eligible for Continuation of Therapy** All target agents are eligible for continuation of therapy 1. Information has been provided that indicates the patient has been treated with the requested agent (starting on samples is not approvable) within the past 90 days **OR** 2. The prescriber states the patient has been treated with the requested agent (starting on samples is not approvable) within the past 90 days AND is at risk if therapy is changed **OR** B. The patient has a diagnosis of chronic kidney disease AND ALL of the following: 1. The patient has been on dialysis for at least 4 months **AND** 2. The patient's hemoglobin was measured in the previous 4 weeks **AND** 3. ONE of the following: A. The patient is currently using an erythropoietin receptor agonist (ESA) (e.g., Aranesp, Epogen, Mircera, Procrit, Retacrit)

Module	Clinical Criteria for Approval
	AND the patient's hemoglobin does NOT exceed 12 g/dL (medical records required) **OR** B. The patient is NOT currently using an ESA AND the patient's hemoglobin is less than or equal to 11 g/dL **AND** 4. The patient's ferritin was measured in the previous 4 weeks **AND** 5. The patient's ferritin is greater than 100 mcg/L **AND** 6. ONE of the following: A. The patient's transferrin saturation (TSAT) is greater than 20% **OR** B. The patient's TSTAT is 20% or lower and is due to recent infection **AND** 7. Other causes of anemia (e.g., pernicious anemia, thalassemia major, sickle cell) have been addressed **OR** C. The patient has another FDA approved indication for the requested agent and route of administration **AND** 2. If the patient has an FDA approved indication, ONE of the following: A. The patient's age is within FDA labeling for the requested indication for the requested agent **OR** B. The prescriber has provided information in support of using the requested agent for the patient's age for the requested indication **AND** 3. The prescriber is a specialist in the area of the patient's diagnosis (e.g., nephrologist) or has consulted with a specialist in the area of the patient's diagnosis **AND** 4. The patient will NOT be using the requested agent in combination with an ESA (e.g., Aranesp, Epogen, Mircera, Procrit, Retacrit) **AND** 5. The patient does NOT have any FDA labeled contraindications to the requested agent **Length of Approval:** 6 months NOTE If Quantity Limit applies, please refer to Quantity Limit criteria **Renewal Evaluation** **Target Agent(s)** will be approved when ALL of the following are met: 1. The patient has been previously approved for the requested agent through the plan's Prior Authorization process **AND** 2. The patient has had clinical benefit with the requested agent (e.g., increase in hemoglobin) **AND** 3. The patient's hemoglobin was measured within the previous 4 weeks **AND** 4. The patient's hemoglobin does NOT exceed 12 g/dL (medical records required) **AND** 5. The prescriber is a specialist in the area of the patient's diagnosis (e.g., nephrologist) or the prescriber has consulted with a specialist in the area of the patient's diagnosis **AND** 6. The patient will NOT be using the requested agent in combination with an ESA (e.g., Aranesp, Epogen, Mircera, Procrit, Retacrit) **AND** 7. The patient does NOT have any FDA labeled contraindications to the requested agent **Length of Approval:** 12 months NOTE If Quantity Limit applies, please refer to Quantity Limit criteria

QUANTITY LIMIT CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
QL with PA	**Evaluation** **Target Agent(s)** will be approved when ONE of the following is met: 1. The requested quantity (dose) does NOT exceed the program quantity limit **OR**

Module	Clinical Criteria for Approval
	2. ALL the following: A. The requested quantity (dose) is greater than the program quantity limit **AND** B. The requested does NOT exceed the maximum FDA labeled dose for the requested indication **AND** C. The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does NOT exceed the program quantity limit