Dojolvi Prior Authorization Program Summary

POLICY REVIEW CYCLE

Effective Date	Date of Origin
01-01-2025	

FDA LABELED INDICATIONS AND DOSAGE

Agent(s)	FDA Indication(s)	Notes	Ref#
Dojolvi® (triheptanoin) Oral liquid	A source of calories and fatty acids for the treatment of pediatric and adult patients with molecularly confirmed long-chain fatty acid oxidation disorders (LC-FAOD)		1

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

CLINICAL RATIONALE

Long Chain Fatty Acid Oxidation Disorders	Long-chain fatty acid oxidation disorders (LC-FAODs) are rare, life-threatening, autosomal recessive genetic disorders characterized by acute crises of energy production and chronic energy deficiency. Patients may present with rhabdomyolysis induced by exercise; fasting or illness; hepatic dysfunction, including severe hypoglycemia and hyperammonemia; and cardiomyopathy. These clinical manifestations can lead to frequent hospitalizations and premature death. LC-FAODs are caused by mutations in nuclear genes encoding mitochondrial enzymes involved in the conversion of dietary long-chain fatty acids (LCFAs) into energy during times of fasting and physiologic stress.(2) Fatty acid oxidation disorders are often captured as part of newborn screenings. A plasma acylcarnitine profile is necessary for diagnosis following an abnormal NBS. DNA testing is considered standard for confirmation and can be helpful in genotype/phenotype correlations. DNA sequencing may reveal variants of uncertain significance, so further investigation of enzyme activity through fibroblast or lymphocyte testing may provide additional information of functional significance.(3,4,5) Current management options leave many patients continuing to experience major clinical events, and mortality rates remain elevated. The current standard therapy for LC-FAODs is avoidance of fasting as well as supplementation of medium-chain triglyceride oil which does not require the typical steps of LC-FAOD for metabolism. Despite this therapy, patients with LC-FAODs continue to experience recurring hospitalizations, and high morbidity and mortality rates. In recent years, the use of medium, odd-chain fatty acids, such as triheptanoin, have been studied as a treatment of LC-FAODs due to its anaplerotic (replenishment of metabolic pathway intermediates) properties. Due to favorable safety and efficacy data from clinical trials, this novel agent has the potential to transform the treatment of LC-FAODs and improve patient outcomes in this patient population.(2,3)
Efficacy	The efficacy of triheptanoin as a source of calories and fatty acids was evaluated in Study 3 (NCT01379625), a 4-month double-blind randomized controlled study comparing triheptanoin (7-carbon chain fatty acid) with trioctanoin (8-carbon chain fatty acid). The study enrolled 32 adult and pediatric patients with a confirmed

	diagnosis of LC-FAOD and evidence of at least one significant episode of rhabdomyolysis and at least two of the following diagnostic criteria: disease specific elevation of acylcarnitines on a newborn blood spot or in plasma, low enzyme activity in cultured fibroblasts, or one or more known pathogenic mutations in CPT2, ACADVL, HADHA, or HADHB. The dosage of study drug was titrated to a protocol-specified target of 20% DCI (actual mean daily dose achieved was 16% for triheptanoin and 14% for trioctanoin). The recommended target dosage of Dojolvi is up to 35% of DCI. After 4 months, patients in both groups had similar mean changes from baseline in left ventricular ejection fraction and wall mass on resting echocardiogram and similar maximal heart rates on treadmill ergometry.(1)
Safety	Triheptanoin carries no contraindications nor boxed warnings.(1)

REFERENCES

Number	Reference
1	Dojolvi prescribing information. Ultragenyx Pharmaceutical Inc. October 2023.
2	Vockley J. Long-Chain Fatty Acid Oxidation Disorders and Current Management Strategies. Am J Manag Care. 2020 Aug;26(7 Suppl):S147-S154.
3	Baker JJ, Burton BK. Diagnosis and Clinical Management of Long-chain Fatty-acid Oxidation Disorders: A Review. TouchREV Endocrinol. 2021 Nov;17(2):108-111.
4	Knottnerus SJG, Bleeker JC, Wust RCI, et al. Disorders of Mitochondrial Long-Chain Fatty Acid Oxidation and the Carnitine Shuttle. Rev Endocr Metab Disord. 2018;19(1):93-106.
5	Merritt JL, Norris M, Kanungo S. Fatty Acid Oxidation Disorders. Ann Transl Med. 2018;6(24):473.

POLICY AGENT SUMMARY PRIOR AUTHORIZATION

Target Brand Agent(s)	Target Generic Agent(s)	Strength	Targeted MSC	Available MSC	Final Age Limit	Preferred Status
Dojolvi	triheptanoin oral liquid	100 %	M ; N ; O ; Y	N		

CLIENT SUMMARY – PRIOR AUTHORIZATION

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Dojolvi	triheptanoin oral liquid	100 %	Accord Enhanced ; Accord Standard ; Choice NetR - A Select ; Choice NetR - F Performance ; Choice NetR-HIM

PRIOR AUTHORIZATION CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
	Initial Evaluation **Target Agent** will be approved when ALL of the following are met: 1. The patient has ONE of the following: A. The patient has a diagnosis of long-chain fatty acid oxidation disorder (LCFAOD) AND ALL of the following: 1. The diagnosis has been confirmed by at least TWO of the following: A. Disease-specific elevations of acylcarnitines on a newborn blood spot or in plasma

Module	Clinical Criteria for Approval
	B. Enzyme activity assay (in cultured fibroblasts or lymphocytes) demonstrating deficiency of an enzyme associated with LCFAODs C. Genetic testing demonstrating pathogenic mutation in a gene associated with LCFAODs **AND** 2. The patient had symptomatic LCFAOD prior to therapy with the requested agent **AND** 3. The patient will not be concurrently using another medium chain triglyceride product **AND** 4. The patient will not be using the requested agent for more than 35% of the patient's total prescribed daily caloric intake **OR** B. The patient has another FDA labeled indication for the requested agent and route of administration **OR** C. The patient has another indication that is supported in compendia for the requested agent and route of administration **AND** 2. The prescriber is a specialist in the area of the patient's diagnosis (e.g., endocrinologist) or the prescriber has consulted with a specialist in the area of the patient's diagnosis **AND** 3. The patient does NOT have any FDA labeled contraindications to the requested agent **Length of Approval:** 12 months **Compendia Allowed:** AHFS, or DrugDex 1 or 2a level of evidence **Renewal Evaluation** **Target Agent** 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 [Note: patients not previously approved for the requested agent will require initial evaluation review] **AND** 2. The patient has had clinical benefit with the requested agent **AND** 3. If the patient has a diagnosis of LCFAOD, BOTH of the following: A. The patient will not be concurrently using another medium chain triglyceride product **AND** B. The patient will not be using the requested agent for more than 35% of the patient's total prescribed daily caloric intake **AND** 4. The prescriber is a specialist in the area of the patient's diagnosis (e.g., endocrinologist) or the prescriber has consulted with a specialist in the area of the patient's diagnosis **AND** 5. The patient does NOT have any FDA labeled contraindications to the requested agent **Length of Approval:** 12 months

Your health benefit plan may not cover certain prescription drug products or drug categories included in this document. Please consult your benefit plan materials for details about your particular benefit. This document may include drugs that are not included on your plan's formulary. For drug coverage status, please consult your plan's formulary.

