



Drug Coverage Policy

Effective Date.....10/01/2025

Coverage Policy Number.....IP0084

Policy Title..... Dojolvi

Metabolic Disorders – Dojolvi

- Dojolvi™ (triheptanoin oral liquid – Ultragenyx)

INSTRUCTIONS FOR USE

The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment where appropriate and have discretion in making individual coverage determinations. Where coverage for care or services does not depend on specific circumstances, reimbursement will only be provided if a requested service(s) is submitted in accordance with the relevant criteria outlined in the applicable Coverage Policy, including covered diagnosis and/or procedure code(s). Reimbursement is not allowed for services when billed for conditions or diagnoses that are not covered under this Coverage Policy (see "Coding Information" below). When billing, providers must use the most appropriate codes as of the effective date of the submission. Claims submitted for services that are not accompanied by covered code(s) under the applicable Coverage Policy will be denied as not covered. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

OVERVIEW

Dojolvi, a synthetic medium odd-chain triglyceride, is indicated as a source of calories and fatty acids for the treatment molecularly confirmed **long-chain fatty acid oxidation disorders (LC-FAODs)** in adults and pediatric patients.¹

For a patient receiving another medium-chain triglyceride product, discontinue prior to the first dose of Dojolvi.

Disease Overview

LC-FAODs are a group of autosomal recessive genetic metabolic disorders in which the body is unable to properly oxidize long-chain fatty acid in the mitochondria (normally an important energy pathway when glucose is low).^{2,3} The four most commonly affected enzymes are carnitine palmitoyl transferase 2 (CPT-2), very long-chain acyl-CoA dehydrogenase (VLCAD), long-chain 3-hydroxyacyl-CoA dehydrogenase (LCHAD), and mitochondrial trifunctional protein (TFP).⁴ Other less common ones may also occur.^{2,4} Onset may occur anywhere from the neonatal period to adulthood. Clinical manifestations are heterogeneous and not well correlated with genotype.² Diagnosis of LC-FAODs has increased with the use of routine newborn screening. Newborn screening tests measure acylcarnitines in dried blood spots.⁵ Abnormal newborn screening results or the presence of symptoms associated with LC-FAODs warrant further evaluation involving plasma acylcarnitine measurement, enzyme activity assays, and/or genetic testing. The activity of specific enzymes can be measured in lymphocytes or skin fibroblasts since these cells express all enzymes involved in long-chain fatty acid oxidation.³ Genetic analysis can identify the specific genetic defect. However, new pathogenic variants are regularly identified, requiring functional studies such as enzyme activity measurements for confirmation of the diagnosis.

Guidelines

A consensus statement regarding treatment recommendations in LC-FAODs was published in 2009; Dojolvi is not specifically addressed, although medium-chain triglycerides are discussed more broadly.⁶ In general, it is noted that the clinical course of LC-FAODs is unpredictable, and medium-chain triglyceride supplementation is an important part of the management strategy for many patients.

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POLICY STATEMENT

Prior Authorization is required for benefit coverage of Dojolvi. All approvals are provided for the duration noted below. Because of the specialized skills required for evaluation and diagnosis of patients treated with Dojolvi as well as the monitoring required for adverse events and long-term efficacy, approval requires Dojolvi to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Documentation: Documentation is required where noted in the criteria as **[documentation required]**. Documentation may include, but is not limited to, chart notes, laboratory tests, claims records, and/or other information.

Dojolvi is considered medically necessary when the following are met:

FDA-Approved Indication

- 1. Long-Chain Fatty Acid Oxidation Disorders.** Approve for 1 year if the patient meets ALL of the following (A, B, C, and D):
 - A)** Patient has a molecularly confirmed diagnosis of a long-chain fatty acid oxidation disorder based on at least TWO of the following (i, ii, or iii):
 - i.** Disease-specific elevations of acylcarnitines on a newborn blood spot or in plasma **[documentation required]**; OR

- ii. Enzyme activity assay (in cultured fibroblasts or lymphocytes) below the lower limit of the normal reference range for the reporting laboratory **[documentation required]**; OR
 Note: Examples of enzyme assays include carnitine palmitoyl transferase 2 (CPT-2), very long-chain acyl-CoA dehydrogenase (VLCAD), long-chain 3-hydroxyacyl-CoA dehydrogenase (LCHAD), and mitochondrial trifunctional protein (TFP).
- iii. Genetic testing demonstrating a pathogenic variant in a gene associated with long-chain fatty acid oxidation disorders **[documentation required]**; AND
 Note: Examples of genes associated with long-chain fatty acid disorders include *CPT2* (encodes CPT-2), *ACADVL* (encodes VLCAD), *HADHA* (encodes LCHAD and TFP), and *HADHB* (encodes TFP).
- B)** Patient will not use any other medium-chain triglyceride products concomitantly with Dojolvi; AND
- C)** Patient meets at least ONE of the following (i, ii, or iii):
 - i. According to the prescriber, the patient has had inadequate efficacy or significant intolerance to an over-the-counter medium-chain triglyceride product (e.g., nutraceutical supplements) [other than Dojolvi]; OR
 - ii. According to the prescriber, the patient has a history of at least one severe or recurrent manifestation of long-chain fatty acid oxidation disorders (i.e., cardiomyopathy, rhabdomyolysis, or hypoglycemia); OR
 - iii. Patient is currently receiving Dojolvi; AND
- D)** The medication is prescribed by or in consultation with a metabolic disease specialist or a physician who specializes in the management of long-chain fatty acid oxidation disorders.

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Receipt of sample product does not satisfy any criteria requirements for coverage.

Conditions Not Covered

Dojolvi for any other use is considered not medically necessary. Criteria will be updated as new published data are available.

References

1. Dojolvi™ oral liquid [prescribing information]. Novato, CA: Ultragenyx; October 2023.
2. Merritt JL II, Norris M, Kanungo S. Fatty acid oxidation disorders. *Ann Transl Med*. 2018;6(24):473.
3. Knotterus SJG, Bleeker JC, Wüst RCI, et al. Disorders of mitochondrial long-chain fatty acid oxidation and the carnitine shuffle. *Rev Endocr Metab Disord*. 2018;19:93-106.
4. Vockley J, Burton B, Berry GT, et al. UX007 for the treatment of long chain-fatty acid oxidation disorders: safety and efficacy in children and adults following 24 weeks of treatment. *Mol Genet Metab*. 2017;120(4):370-77.
5. ACT Sheets and Algorithms: Newborn Screening ACT Sheets and Algorithms. American College of Molecular Genetics and Genomics. Available at: https://www.acmg.net/ACMG/Medical-Genetics-Practice-Resources/ACT_Sheets_and_Algorithms.aspx. Accessed on July 08, 2025.

6. Spiekerkoetter U, Lindner M, Santer R, et al. Treatment recommendations in long-chain fatty acid oxidation defects: consensus from a workshop. *J Inherit Metab Dis*. 2009;32(4):498-505.

Revision Details

Type of Revision	Summary of Changes	Date
Annual Revision	Policy Name: Updated title from "Triheptanoin" to "Metabolic Disorders – Dojolvi." Long-Chain Fatty Acid Oxidation Disorders: For diagnosis by genetic testing, rephrased the term "mutation" to "variant." Added "according to the prescriber" in the criteria stating that the patient must have inadequate efficacy or significant intolerance to an over-the-counter medium-chain triglyceride product or has a history of at least one severe or recurrent manifestation of long-chain fatty acid oxidation.	11/01/2024
Annual Revision	Added a policy statement. Added documentation requirements. Updated the conditions not covered statement.	10/01/2025

The policy effective date is in force until updated or retired.

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