

## PRIOR AUTHORIZATION POLICY

**POLICY:** Metabolic Disorders – Dojolvi Prior Authorization Policy

- Dojolvi™ (triheptanoin oral liquid – Ultragenyx)

**REVIEW DATE:** 07/31/2024

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### OVERVIEW

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

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).<sup>2,3</sup> 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).<sup>4</sup> Other less common ones may also occur.<sup>2,4</sup> Onset may occur anywhere from the neonatal period to adulthood. Clinical manifestations are heterogeneous and not well correlated with genotype.<sup>2</sup> Diagnosis of LC-FAODs has increased with the use of routine newborn screening. Newborn screening tests measure acylcarnitines in dried blood spots.<sup>5</sup> 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.<sup>3</sup> 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.<sup>6</sup> 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.

### POLICY STATEMENT

Prior Authorization is recommended for prescription 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.

**Automation:** None.

### RECOMMENDED AUTHORIZATION CRITERIA

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Coverage of Dojolvi is recommended in those who meet the following criteria:

### 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; OR
    - ii. Enzyme activity assay (in cultured fibroblasts or lymphocytes) below the lower limit of the normal reference range for the reporting laboratory; 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; 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 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.

### CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Dojolvi is not recommended in the following situations:

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. 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](https://www.acmg.net/ACMG/Medical-Genetics-Practice-Resources/ACT_Sheets_and_Algorithms.aspx). Accessed on July 22, 2024.
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.

