

## PRIOR AUTHORIZATION POLICY

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

- Dojolvi™ (triheptanoin oral liquid – Ultragenyx)

**REVIEW DATE:** 07/22/2020; selected revision 11/11/2020

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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 patients 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 mutations 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> Mutation analysis can identify the specific genetic defect. However, new mutations and 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 (MCT) are discussed more broadly.<sup>6</sup> Dietary recommendations are provided for VLCAD deficiency but it is noted that these can also be applied to similar disorders, such as CPT-2 deficiency. For symptomatic patients with VLCAD deficiency, long-chain fat content of the diet is suggested to be 25% to 30% of total energy. The diet should be enriched with MCT to provide 20% of total energy from MCT. In asymptomatic VLCAD deficiency, the necessity of dietary long-chain fat restriction is under debate. Per the consensus statement, the current recommendation is to mildly reduce fat content to 30% to 40% of total energy in these patients. However, it is noted that the clinical course is not predictable. Even for patients in whom long-chain triglyceride restriction is deemed unnecessary, MCT supplementation (especially prior to exercise) may still be needed. For LCHAD and TFP deficiency, both symptomatic and asymptomatic patients should follow long-chain fat restriction with MCT supplementation.

### 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

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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

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

#### FDA-Approved Indications

- 1. Long-Chain Fatty Acid Oxidation Disorders.** Approve for 1 year if the patient meets the following criteria (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 (TWO of 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 pathogenic mutation 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 (nutraceutical supplements) medium-chain triglyceride product (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.

**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™ [prescribing information]. Novato, CA: Ultragenyx; June 2020.
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 6, 2020.
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.

**HISTORY**

Type of Revision	Summary of Changes	Review Date
New Policy	--	07/22/2020
Selected Revision	<b>Long-Chain Fatty Acid Oxidation Disorders:</b> Criteria were added requiring that the patient meet one of the following: inadequate efficacy or significant intolerance to over-the-counter (nutraceutical) medium-chain triglyceride supplements; a history of at least one severe or recurrent manifestation of long-chain fatty acid oxidation disorders; or currently receiving Dojolvi.	11/11/2020