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Coverage Policy Number **IP0084**

Triheptanoin

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Related Coverage Resources

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. 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

This policy supports medical necessity review for **Dojolvi**™ (triheptanoin oral liquid).

Medical Necessity Criteria

Triheptanoin oral liquid (Dojolvi) is considered medically necessary when the following are met:

1. **Long-Chain Fatty Acid Oxidation Disorders. Individual meets ALL of the following criteria:**
   A. Individual has a molecularly confirmed diagnosis of a long-chain fatty acid oxidation disorder based on at least **TWO** of the following:
      i. Disease-specific elevations of acylcarnitines on a newborn blood spot or in plasma
      ii. Enzyme activity assay (in cultured fibroblasts or lymphocytes) below the lower limit of the normal reference range for the reporting laboratory [for example, 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 [for example, *CPT2* (encodes CPT-2), *ACADVL* (encodes VLCAD), *HADHA* (encodes LCHAD and TFP), and *HADHB* (encodes TFP)]

B. Individual will not use any other medium-chain triglyceride products concomitantly with Dojolvi
C. Individual meets at least **ONE** of the following:
   i. Individual has had inadequate efficacy or significant intolerance to an over-the-counter (nutraceutical supplements) medium-chain triglyceride product
   ii. Individual has a history of at least one severe or recurrent manifestation of long-chain fatty acid oxidation disorders (for example, cardiomyopathy, rhabdomyolysis, or hypoglycemia)
   iii. Individual is currently receiving Dojolvi
D. 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.

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

Reauthorization Criteria

Triheptanoin oral liquid (Dojolvi) is considered medically necessary for continued use when initial criteria are met AND there is documentation of beneficial response.

Authorization Duration

Initial approval duration is up to 12 months.

Reauthorization approval duration is up to 12 months.

Conditions Not Covered

Dojolvi (triheptanoin oral liquid) is considered experimental, investigational or unproven for ANY other use.

Background

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).[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 mutations 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] 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 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.

References

1. Dojolvi™ oral liquid [prescribing information]. Novato, CA: Ultragenyx; November 2021.
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 18, 2023.
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.