Drug and Biologic Coverage Policy

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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).

Coverage Policy

Triheptanoin oral liquid (Dojolvi) is considered medically necessary when ALL of the following are met:
1. The individual has a molecularly confirmed diagnosis of a long-chain fatty acid oxidation disorder based on at least TWO of the following:
   a. Disease-specific elevations of acylcarnitines on a newborn blood spot or in plasma
   b. Enzyme activity assay (in cultured fibroblasts or lymphocytes) below the lower limit of the normal reference range for the reporting laboratory [for example, carnitine palmityl transferase 2 (CPT-2), very long-chain acyl-CoA dehydrogenase (VLCAD), long-chain 3-hydroxyacyl-CoA dehydrogenase (LCHAD), and mitochondrial trifunctional protein (TFP)]
   c. 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)]
2. Individual will not use any other medium-chain triglyceride products concomitantly with Dojolvi
3. The Individual meets at least ONE of the following:
   a. According to the healthcare professional, the individual has had inadequate efficacy or significant intolerance to an over-the-counter (nutraceutical supplements) medium-chain triglyceride product
   b. According to the healthcare professional, the 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)
   c. The individual is currently receiving Dojolvi
4. Dojolvi 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.

**Documentation:** When documentation is required, the prescriber must provide written documentation supporting the trials of these other agents. Documentation may include, but is not limited to, chart notes, prescription claims records, and/or prescription receipts

**Reauthorization Criteria**

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

**Authorization Duration**

Initial approval and reauthorization duration is 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 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).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 (MCT) are discussed more broadly.\(^6\) 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.

**References**