09-J3000-87

Original Effective Date: 01/01/21

Reviewed: 12/10/25

Revised: 01/15/26

Subject: Triheptanoin (Dojolvi®) Oral Liquid

THIS MEDICAL COVERAGE GUIDELINE IS NOT AN AUTHORIZATION, CERTIFICATION, EXPLANATION OF BENEFITS, OR A GUARANTEE OF PAYMENT, NOR DOES IT SUBSTITUTE FOR OR CONSTITUTE MEDICAL ADVICE. ALL MEDICAL DECISIONS ARE SOLELY THE RESPONSIBILITY OF THE PATIENT AND PHYSICIAN. BENEFITS ARE DETERMINED BY THE GROUP CONTRACT, MEMBER BENEFIT BOOKLET, AND/OR INDIVIDUAL SUBSCRIBER CERTIFICATE IN EFFECT AT THE TIME SERVICES WERE RENDERED. THIS MEDICAL COVERAGE GUIDELINE APPLIES TO ALL LINES OF BUSINESS UNLESS OTHERWISE NOTED IN THE PROGRAM EXCEPTIONS SECTION.

DESCRIPTION:

Triheptanoin (Dojolvi) is a medium-chain triglyceride that was approved by the US Food and Drug Administration (FDA) in June 2020 and is indicated as a source of calories and fatty acids for the treatment of pediatric and adult patients with molecularly confirmed long-chain fatty acid oxidation disorders (LC-FAOD). Triheptanoin is the first FDA-approved therapy for LC-FAOD. Dojolvi, as sponsored by the innovator drug company, was previously granted orphan drug designation for the treatment of fatty acid oxidation disorders in 2015. Dojolvi is a highly purified, synthetic, 7-carbon fatty acid triglyceride specifically designed to provide medium-chain, odd-carbon fatty acids that are metabolized to bypass faulty pathways and provide an alternative energy source for people with LC-FAOD.

Long-chain fatty acid oxidation disorders (LC-FAOD) is one of the most severe categories of fatty acid oxidation disorders (FAOD) and often present within a few days of life, though milder disease can have an onset in adolescents or adulthood. LC-FAOD consists of a family of rare genetic disorders caused by impaired fatty acid metabolism pathways. It is estimated that 2,000 to 3,500 people are living with LC-FAOD in the US, and an estimated 100 births per year are diagnosed with confirmed LC-FAOD in the US. Patients with LC-FAOD can present with a wide range of symptoms varying from severe neonatal hypoglycemia to cardiomyopathy, sometimes leading to sudden death. Milder adolescent and adult phenotypes can present with recurrent rhabdomyolysis and exercise intolerance. The most common chronic manifestations are frequent episodes of myalgia, recurrent rhabdomyolysis induced by exercise, fasting or illness, and cardiomyopathy, which can often lead to significant morbidities and life-threatening complications. Although newborn screenings and early intervention have reduced mortality, many patients continue to experience frequent hospitalizations and significant morbidity despite dietary treatment. Management of LC-FAOD includes avoidance of fasting, providing a long-chain fat-restricted diet, carnitine supplementation in some cases, and supplementation with medium-chain triglycerides (MCTs), a fat source that does not require long-chain fatty acid oxidation for its metabolism. MCT oil is

currently available as a medical food product. Despite treatment, many patients still experience frequent hospitalizations and significant morbidity.

The efficacy of triheptanoin as a source of calories and fatty acids was evaluated in a 4-month double-blind randomized controlled study comparing triheptanoin (7-carbon chain fatty acid) with trioctanoin (8-carbon chain fatty acid). The study enrolled 32 adult and pediatric patients with a confirmed diagnosis of LC-FAOD and evidence of at least one significant episode of rhabdomyolysis and at least two of the following diagnostic criteria: disease specific elevation of acylcarnitines on a newborn blood spot or in plasma, low enzyme activity in cultured fibroblasts, or one or more known pathogenic mutations in CPT2, ACADVL, HADHA, or HADHB. The dosage of study drug was titrated to a protocol-specified target of 20% DCI (actual mean daily dose achieved was 16% for triheptanoin and 14% for trioctanoin). Patients ranged in age from 7 years to 64 years (median 24 years) and 12 were male. Baseline cardiovascular function in both groups was normal and within test/retest variability normally observed in repeated echocardiograms. After 4 months, patients in both groups had similar mean changes from baseline in left ventricular ejection fraction and wall mass on resting echocardiogram and similar maximal heart rates on treadmill ergometry. Five patients experienced 7 events of rhabdomyolysis in the triheptanoin group, and 4 patients experienced 7 events of rhabdomyolysis in the trioctanoin group. No differences were observed between triheptanoin and trioctanoin groups in blood markers of metabolism including glucose, insulin, lactate, total serum, ketones, acylcarnitines, and serum-free fatty acid concentrations.

The safety population for triheptanoin included 79 patients with LC-FAOD in two studies: one open-label 78-week study in 29 patients (Study 1; NCT01886378) followed by an open-label extension study (Study 2; NCT02214160). Twenty-four patients from Study 1 continued into Study 2. Patients ranged from 4 months to 63 years of age. The daily dosage of triheptanoin ranged between 12% and 41% DCI (which corresponds to 0.7 g/kg/day to 6.0 g/kg/day for pediatric patients and 0.5 g/kg/day to 1.3 g/kg/day for adult patients) for a mean duration of 23 months. The most common adverse reactions to DOJOLVI reported in the pooled safety population were gastrointestinal (GI)-related, and included abdominal pain (abdominal discomfort, abdominal pain, abdominal distension, abdominal pain upper, GI pain) [60%], diarrhea [44%], vomiting [44%], and nausea [14%]. The median time to onset of a first occurrence of a GI adverse reaction was 7.3 weeks. GI adverse reactions led to dose reductions in 35% and 12% of patients in Study 1 and Study 2, respectively.

POSITION STATEMENT:

Comparative Effectiveness

The FDA has deemed the drug(s) or biological product(s) in this coverage policy to be appropriate for self-administration or administration by a caregiver (i.e., not a healthcare professional). Therefore, coverage (i.e., administration) in a provider-administered setting such as an outpatient hospital, ambulatory surgical suite, physician office, or emergency facility is not considered medically necessary.

Initiation of triheptanoin (Dojolvi) oral liquid **meets the definition of medical necessity** when **ALL** of the following are met ("1" to "8"):

1. Member has a diagnosis of a long-chain fatty acid oxidation disorder (LC-FAOD) [e.g., carnitine-acylcarnitine translocase (CACT) deficiency, carnitine palmitoyltransferase 1 (CPT1) deficiency,

carnitine palmitoyltransferase 2 (CPT2) deficiency, long-chain 3-hydroxy-acyl-CoA dehydrogenase (LCHAD) deficiency, trifunctional protein (TFP) deficiency, very long-chain acyl-CoA dehydrogenase (VLCAD) deficiency]

2. Genetic and/or molecular testing has been completed to confirm the diagnosis (e.g., positive for pathogenic mutations in *CPT1A, CPT2, ACADVL, HADHA*, or *HADHB* gene) – documentation of the test results must be submitted
3. Member is currently managed on a stable treatment regimen (including diet) for their LC-FAOD, which may include a low-fat, high-carbohydrate diet; avoidance of fasting; and/or medium-chain triglyceride (MCT) oil
4. Triheptanoin is prescribed by, or in consultation with, a specialist with experience in the management of fatty acid oxidation disorders
5. Triheptanoin will **NOT** be used in combination with another medium-chain triglyceride (MCT) product
6. Triheptanoin will **NOT** be used in combination with a pancreatic lipase inhibitor (e.g., orlistat)
7. Member does **NOT** have pancreatic insufficiency
8. Dosage of triheptanoin does not exceed 35% of the patient's total prescribed daily caloric intake (DCI) divided into at least four doses [the total daily dosage (mL) = patients DCI (kcal) x target % dose of DCI divided by 8.3 kcal/mL of triheptanoin].

Approval duration: 12 months

Continuation of triheptanoin (Dojolvi) oral liquid **meets the definition of medical necessity** when **ALL** of the following criteria are met ("1" to "7"):

1. An authorization or reauthorization for triheptanoin has been previously approved by Florida Blue or another health plan in the past 2 years for the treatment of LC-FAOD (if another health plan, documentation of a health plan-paid claim for triheptanoin during the 90 days immediately before the request must be submitted), **OR** the member previously met **ALL** indication-specific initiation criteria
2. Member has had clinical improvement compared to baseline (e.g., gross motor development/motor function for infants/young children, exercise tolerance and endurance for older children and adults, and decrease in frequency of hypoglycemia, rhabdomyolysis, and exacerbation of cardiomyopathy)
3. Triheptanoin is prescribed by, or in consultation with, a specialist with experience in the management of fatty acid oxidation disorders
4. Triheptanoin is **NOT** being used in combination with another medium-chain triglyceride (MCT) product
5. Triheptanoin will **NOT** be used in combination with a pancreatic lipase inhibitor (e.g., orlistat)
6. Member does **NOT** have pancreatic insufficiency
7. Dosage of triheptanoin does not exceed 35% of the patient's total prescribed daily caloric intake (DCI) divided into at least four doses [the total daily dosage (mL) = patients DCI (kcal) x target % dose of DCI divided by 8.3 kcal/mL of triheptanoin].

Approval duration: 12 months

DOSAGE/ADMINISTRATION:

THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER'S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.

FDA-approved

- Indicated as a source of calories and fatty acids for the treatment of pediatric and adult patients with molecularly confirmed long-chain fatty acid oxidation disorders (LC-FAOD).
- Assess metabolic requirements by determining daily caloric intake (DCI) prior to calculating the dosage of triheptanoin. The total daily dosage (mL) = patients DCI (kcal) x target % dose of DCI divided by 8.3 kcal/mL of triheptanoin. For patients receiving another medium-chain triglyceride (MCT) product, discontinue prior to the first dose of triheptanoin.
- The recommended target daily dosage is up to 35% of the patient's total prescribed DCI divided into at least four doses and administered orally diluted with foods, liquids, or formula via a silicone or polyurethane feeding tube. In order to reach a target daily dosage, patients may require an increase in their total fat intake. All patients should be under the care of a clinical specialist knowledgeable in appropriate disease-related dietary management based upon current nutritional recommendations.
    - For patients not currently taking a MCT product - Initiate triheptanoin at a total daily dosage of approximately 10% DCI divided into at least four times per day and increase to the recommended total daily dosage of up to 35% DCI over a period of 2 to 3 weeks.
    - For patients switching from another MCT product - Initiate triheptanoin at the last tolerated daily dosage of MCT divided into at least four times per day. Increase the total daily dosage by approximately 5% DCI every 2 to 3 days until the target dosage of up to 35% DCI is achieved.
- Refer to the full prescribing information for instructions on how to prepare and administer.

Dose Adjustments

- If a patient has difficulty tolerating 1/4 of the total daily dosage at one time, more frequent smaller doses may be considered.
- If a patient experiences gastrointestinal adverse reaction(s), consider dosage reduction until the gastrointestinal symptoms resolve.

Drug Availability

- Clear, colorless to light yellow oral liquid supplied in 500 mL bottles containing 100% w/w of triheptanoin.
- Store at 20° to 25°C (68° to 77°F); excursions permitted to 15° to 30°C (59° to 86°F). Do not freeze.
- Opened bottles can be used for up to 9 months after opening, but not beyond the expiration date on the bottle. Do not dose or store using materials made of polystyrene or polyvinyl chloride (PVC) containers.

PRECAUTIONS:

Boxed Warning

- None

Contraindications

- None

Precautions/Warnings

- **Feeding Tube Dysfunction**: Feeding tube performance and functionality can degrade over time depending on usage and environmental conditions. In clinical trials, feeding tube dysfunction was reported in patients receiving triheptanoin. The contribution of triheptanoin cannot be ruled out. Do not administer triheptanoin in feeding tubes manufactured of polyvinyl chloride (PVC). Regularly monitor the feeding tube to ensure proper functioning and integrity.
- **Intestinal Malabsorption in Patients with Pancreatic Insufficiency**: Pancreatic enzymes hydrolyze triheptanoin and release heptanoate as medium-chain fatty acids in the small intestine. Low or absent pancreatic enzymes may result in reduced absorption of heptanoate subsequently leading to insufficient supplementation of medium-chain fatty acids. Avoid administration of triheptanoin in patients with pancreatic insufficiency.
- **Drug Interaction with Pancreatic Lipase Inhibitors**: Co-administration of triheptanoin with a pancreatic lipase inhibitor (e.g., orlistat) may reduce exposure to the triheptanoin metabolite, heptanoate, and reduce the clinical effect of triheptanoin. Avoid co-administration of triheptanoin with pancreatic lipase inhibitors.

BILLING/CODING INFORMATION:

HCPCS Coding

J8499	Prescription drug, oral, non chemotherapeutic, nos

ICD-10 Diagnosis Codes That Support Medical Necessity

E71.310	Long chain/very long chain acyl CoA dehydrogenase deficiency
E71.314	Muscle carnitine palmitoyltransferase deficiency

REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT**.

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Part D: Florida Blue has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline.

Medicare Advantage: No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of guideline creation.

If this Medical Coverage Guideline contains a step therapy requirement, in compliance with Florida law 627.42393, members or providers may request a step therapy protocol exemption to this requirement if

based on medical necessity. The process for requesting a protocol exemption can be found at Coverage Protocol Exemption Request.

DEFINITIONS:

None

RELATED GUIDELINES:

None

OTHER:

None

REFERENCES:

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2. ClinicalTrials.gov. An Open-label Phase 2 Study of UX007 (Triheptanoin) in Subjects with Long-Chain Fatty Acid Oxidation Disorders (LC-FAOD). NCT01886378. Available at: https://clinicaltrials.gov/ct2/show/NCT01886378. Accessed 12/2/20.
3. ClinicalTrials.gov. Long-Chain Fatty Acid Oxidation Disorders (LC-FAOD) Extension Study for Subjects Previously Enrolled in Triheptanoin Studies. NCT02214160. Available at: https://clinicaltrials.gov/ct2/show/NCT02214160. Accessed 12/2/20.
4. Dojolvi (triheptanoin liquid) [package insert]. Novato, CA: Ultragenyx Pharmaceutical Inc. October 2023.
5. FDA Orphan Drug Designations and Approvals [Internet]. Washington, D.C. Available at: http://www.accessdata.fda.gov/scripts/opdlisting/oopd/. Accessed 11/21/25.
6. Gillingham MB, Heitner SB, Martin J, et al. Triheptanoin versus trioctanoin for long- chain fatty acid oxidation disorders: a double blinded, randomized controlled trial. JInherit Metab Dis. 2017;40(6):831-843.
7. Micromedex Healthcare Series [Internet Database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed 11/21/25.
8. 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; 120:370-377.
9. Vockley J, Burton B, Berry GT, et al. Results from a 78-week single-arm, open-label Phase 2 study to evaluate UX007 in pediatric and adult patients with severe long-chain fatty acid oxidation disorders (LC-FAOD). J Inherit Metab Dis 2019; 42:169-177.

COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee 12/10/25.

GUIDELINE UPDATE INFORMATION:

01/01/21	New Medical Coverage Guideline.
01/15/23	Review and revision to guidelines consisting of updating the references.
01/15/24	Review and revision to guidelines consisting of updating the references.
01/15/25	Review and revision to guidelines consisting of updating the references.
01/15/26	Review and revision to guidelines consisting of updating the references.