triheptanoin oral liquid (Dojolvi™)

Policy # 00735
Original Effective Date: 03/08/2021
Current Effective Date: 03/10/2025

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc.(collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider triheptanoin oral liquid (Dojolvi™)‡ for the treatment of molecularly confirmed long-chain fatty acid oxidation disorders (LC-FAOD) to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility for triheptanoin oral liquid (Dojolvi) will be considered when the following criteria are met:

- Patient has a diagnosis of Long-Chain Fatty Acid Oxidation Disorder; AND
- Patient will NOT be using any other medium chain triglyceride products concurrently with the requested drug; AND
- Total daily dosage should not exceed 35% of the patient's total prescribed daily caloric intake; AND
- Patient is under the care of a clinical specialist knowledgeable in appropriate disease-related dietary management based upon current nutritional recommendations; AND
- Patient meets TWO of the following three items:
    - Patient has disease specific elevations of acylcarnitines on a newborn blood spot or in plasma.
    - Patient has an enzyme activity assay (in cultured fibroblasts or lymphocytes) below the lower limit of the normal reference range for the reporting laboratory.
    - Patient has one or more known pathogenic mutations in *CPT2*, *ACADVL*, *HADHA*, or *HADHB* confirmed via genetic testing.

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When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of triheptanoin oral liquid (Dojolvi) when the patient selection criteria are not met to be **investigational.***

Background/Overview

Dojolvi is a medium-chain triglyceride 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. Dosing is based on daily caloric intake calculations and varies per individual and situation, but the targeted total daily dose should not exceed 35% of the patient's prescribed daily caloric intake. Dojolvi is administered either mixed with semi-solid food or liquids orally or enterally via a silicone or polyurethane feeding tube. The package insert also states that any patient on Dojolvi needs to be under the care of a clinical specialist knowledgeable in appropriate disease-related dietary management based upon current nutritional recommendations. The package insert also specifies that other medium-chain triglyceride product should be discontinued prior to the first dose of Dojolvi.

Long-chain fatty acid oxidation disorders are caused by the body's inability to properly oxidize long-chain fatty acids in the mitochondria. This is an important energy pathway, particularly when blood glucose is low. These disorders are autosomal recessive genetic disorders. More than 15 enzymes are involved in long-chain fatty acid oxidation, and a genetic deficiency in any of the enzymes can lead to a long-chain fatty acid oxidation disorder. Symptoms of this condition typically exacerbate during low-energy states (fasting, exercise, and illness). Typical symptoms include hypoglycemia, cardiomyopathy (potentially fatal), and myopathy. Dojolvi is currently the first and only product that is FDA approved for this condition, however there are medium-chain triglyceride supplements available over the counter. However, as seen in Dojolvi's comparison to a supplement, the statistical significance between the two products was not realized.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

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Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

The efficacy of Dojolvi as a source of calories and fatty acids was evaluated in Study 3, a 4-month double-blind randomized controlled study comparing Dojolvi (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 new born 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 Dojolvi and 14% for trioctanoin). The recommended target dosage of Dojolvi is up to 35% of daily caloric intake (DCI).

Primary outcomes included changes in total energy expenditure, cardiac function by echocardiogram, exercise tolerance, and phosphocreatine recovery following acute exercise 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. Left ventricular ejection fraction (LVEF) increased by 4.2% with Dojolvi vs. baseline and decreased by 3.1% with trioctanoin vs. baseline. However, note that statistical significance was not observed between the two groups.

References

1. Dojolvi [package insert]. Ultragenyx Pharmaceutical, Incorporated. Updated September 2020.
2. Dojolvi Drug Evaluation. Express Scripts. Updated July 2020.
3. Overview of Fatty Acid Oxidation Disorders. UpToDate. Accessed January 11, 2021.

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Policy History

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02/04/2021	Medical Policy Committee review
02/10/2021	Medical Policy Implementation Committee approval. New policy.
02/03/2022	Medical Policy Committee review
02/09/2022	Medical Policy Implementation Committee approval. No change to coverage.
02/02/2023	Medical Policy Committee review
02/08/2023	Medical Policy Implementation Committee approval. No change to coverage.
02/01/2024	Medical Policy Committee review
02/14/2024	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
02/06/2025	Medical Policy Committee review
02/12/2025	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.

Next Scheduled Review Date: 02/2026

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
    1. Consultation with technology evaluation center(s);
    2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
    3. Reference to federal regulations.

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;

B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: If the Patient's health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

NOTICE: Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage.