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Dojolvi (triheptanoin)

NOTICE

This policy contains information which is clinical in nature. The policy is not medical advice. The information in this policy is used by Wellmark to make determinations whether medical treatment is covered under the terms of a Wellmark member's health benefit plan. Physicians and other health care providers are responsible for medical advice and treatment. If you have specific health care needs, you should consult an appropriate health care professional. If you would like to request an accessible version of this document, please contact customer service at 800-524-9242.

BENEFIT APPLICATION

Benefit determinations are based on the applicable contract language in effect at the time the services were rendered. Exclusions, limitations, or exceptions may apply. Benefits may vary based on contract, and individual member benefits must be verified. Wellmark determines medical necessity only if the benefit exists and no contract exclusions are applicable. This medical policy may not apply to FEP. Benefits are determined by the Federal Employee Program.

DESCRIPTION

The indications below including FDA-approved indications and compendial uses are considered covered benefits provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Dojolvi 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).

POLICY

Required Documentation

Submission of the following information is necessary to initiate the prior authorization review:

- A. Chart note documentation of at least one hospitalization or ER visit within the past year due to rhabdomyolysis, cardiomyopathy, or hypoglycemic episodes.
- B. Chart or laboratory documentation of low enzyme activity in cultured fibroblasts and/or pathogenic mutations confirmed by genetic testing as required in the Criteria for Initial Approval.

Criteria for Initial Approval

Long-chain fatty acid oxidation disorders (LC-FAOD)

Authorization of **6 months** may be granted for treatment of long-chain fatty acid oxidation disorders when all of the following criteria are met:

- A. Member has a diagnosis of carnitine palmitoyltransferase type 2 (CPT2) deficiency, very-long-chain acyl-CoA dehydrogenase (VLCAD) deficiency, long-chain L-3 hydroxyacyl-CoA dehydrogenase deficiency (LCHAD) or trifunctional protein (TFP) deficiency

- B. Member has been receiving a low-fat/high-carbohydrate diet and medium-chain triglyceride (MCT) supplementation (e.g., MCT oil supplements, specialized infant or pediatric formula supplemented with MCT for LC-FAOD such as Lipistart, Monogen, Portagen, Enfaport, MCT Procal, MCT Oil, and Liquigen).
- C. Member has experienced at least one hospitalization or ER visit within the past year due to any of the following events: rhabdomyolysis, cardiomyopathy, or hypoglycemic episodes.
- D. At least two of the following diagnostic criteria are met:
 1. Elevated acylcarnitine level on a newborn blood spot or in plasma, as applicable to the specific disease:
 - a. CPT2 deficiency: elevated C16 and/or C18:1
 - b. LCHAD and TFP deficiency: elevated C16-OH and/or C18 and other acylcarnitines
 - c. VLCAD deficiency: elevated C14:1 and/or other long-chain acylcarnitines
 2. Low enzyme activity in cultured fibroblasts
 3. One or more known pathogenic mutations in CPT2, acyl-CoA dehydrogenase very-long-chain (ACADVL), hydroxyacyl-CoA dehydrogenase trifunctional multienzyme complex subunit alpha (HADHA) or hydroxyacyl-CoA dehydrogenase trifunctional multienzyme complex subunit beta (HADHB) gene

Continuation of Therapy

Authorization of **12 months** may be granted for members with an indication listed in the Criteria for Initial Approval who are currently receiving the requested medication through a paid pharmacy or medical benefit, and who are experiencing benefit from therapy as evidenced by disease stability or disease improvement (e.g., improvement in cardiomyopathy, glycemic control or exercise tolerance, or a reduction in episodes of cardiomyopathy, rhabdomyolysis, hypoglycemia or hospitalizations).

Dosing and Administration

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines.

CLINICAL RATIONALE

Background

LC-FAODs are rare, autosomal recessive disorders caused by defects in the metabolic pathway that convert fatty acids into energy. LC-FAODs are caused by defects in genes that encode six mitochondrial enzymes involved in the oxidation of long-chain fats for energy: carnitine palmitoyl transferase 1 (CPT1), CPT2, carnitine/acylcarnitine translocase (CACT), VLCAD, LCHAD, and TFP. Partial or incomplete oxidation of fatty acids due to a deficiency of one of these enzymes results in the accumulation of high concentrations of potentially toxic fatty acid intermediates and an energy deficit state in numerous organ systems, particularly during times of physiologic stress or fasting. Clinical manifestations of LC-FAODs can include rhabdomyolysis, liver dysfunction, severe hypoglycemia, and cardiomyopathy. Early in life, the main presentations involve the liver, skeletal muscle, or heart due to hypoglycemia and liver dysfunction. Muscle weakness and rhabdomyolysis are common manifestations later in life; episodic cardiomyopathy with or without arrhythmias can be present at any age. Management of LC-FAODs includes the avoidance of fasting, the maintenance of a low-fat/high carbohydrate diet, and supplementation with MCTs to circumvent the defect in the degradation of long-chain fatty acids. Dojolvi is a medium-chain triglyceride (MCT) consisting of three odd-chain seven-carbon length fatty acids (heptanoate) that provide a source of calories and fatty acids to bypass the enzyme deficiencies associated with LC-FAODs for energy production and replacement. It is the first FDA-approved product for the treatment of LC-FAODs.

Efficacy

The efficacy of Dojolvi for the treatment of LC-FAODs was evaluated in 32 patients in a phase II, double-blind, parallel-design, randomized, active-controlled trial that took place over 78 weeks. The study enrolled both adult and pediatric patients with LC-FAOD that were randomized to receive triheptanoin (7-carbon

chain fatty acid) or trioctanoin (8-carbon chain fatty acid). Primary outcomes included changes in total energy expenditure (TEE), cardiac function as measured by echocardiogram, exercise tolerance, and phosphocreatine recovery following acute exercise after four months of treatment. Secondary endpoints included body composition, blood biomarkers, and adverse events. After 4 months of treatment, there was no significant difference in total energy expenditure or phosphocreatine recovery following acute exercise between the treatment groups. The relative change in left ventricular ejection fraction from baseline was greater by 7.4%, in the Dojolvi group compared with the trioctanoin group (95% of baseline CI -0.1 to 15; p = 0.046). Of note, the majority of the observed changes in ejection fraction occurred within the normal range, and the majority of patients in the trial had normal cardiac function at baseline. Maximum heart rate during moderate intensity treadmill exercise test decreased in patients treated with Dojolvi and was significantly lower by a mean 6.98 beats per minute compared with patients in the trioctanoin group (95% CI 0.34 to 13.63; p = 0.040). There were also no significant between-group differences in blood biomarkers of metabolism, including glucose, insulin, lactate, total serum ketones, acylcarnitines, and serum free fatty acid concentrations. Overall, adverse events related to supplementation with Dojolvi or trioctanoin were minor and predominantly consisted of gastrointestinal upset; there was no significant difference in reported gastrointestinal adverse events or incidence of rhabdomyolysis. There were seven hospitalizations for acute rhabdomyolysis in both the Dojolvi and trioctanoin groups.

Safety

Warnings and precautions for Dojolvi include feeding tube dysfunction and intestinal malabsorption in patients with pancreatic insufficiency. The most common adverse reactions that occurred in ≥ 14% of patients in clinical trials were abdominal pain, diarrhea, vomiting, and nausea.

PROCEDURES AND BILLING CODES

To report provider services, use appropriate CPT* codes, Alpha Numeric (HCPCS level 2) codes, Revenue codes, and/or ICD diagnostic codes.

- N/A

REFERENCES

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POLICY HISTORY

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