MN.024.A Relizorb®

Original Implementation Date : 03/22/2023
Version [A] Date : 03/20/2024
Last Reviewed Date: 02/19/2025

PRODUCT VARIATIONS

This policy applies to all Jefferson Health Plans/Health Partners Plans lines of business unless noted below.

POLICY STATEMENT

We consider Relizorb® medically necessary for its Food and Drug Administration U.S. Food and Drug Administration (FDA) approved indications when the prior authorization criteria listed in this policy are met.

POLICY GUIDELINES

Indicated for adults and pediatric patients (2 years and older) to help break down (digest) the fats in enteral tube feeding formula into an absorbable form the body can use.

Prior Authorization Criteria

1. Is the patient 2 years of age and above? *If YES, go to 2. If NO, refer to the Medical Director.*

2. Does this patient have a diagnosis of cystic fibrosis? *If YES, go to 3. If NO, refer to the Medical Director.*

3. Does the patient present clinical signs and symptoms of impaired digestion, malabsorption, or nutritional risk, as indicated by weight loss that presents actual or potential for developing, malnutrition as defined as:

In children (5 to 18 years of age) with ONE of the following:

1. No weight gain or an abnormally slow rate of gain for three months for children older than 5 years.

2. Weight for height less than the 10th percentile, abnormal laboratory tests pertinent to the diagnosis and risk factors for actual or potential malnutrition have been identified and documented.

   If YES, go to 4. If NO, refer to the Medical Director.

4. Does the patient have a recent (within the past year) comprehensive medical history and a physical examination? *If YES, go to 5. If NO, refer to the Medical Director.*

5. Does the patient have a written plan of care that has been developed for regular monitoring of signs and symptoms to detect improvement in the person's condition? *If YES, go to 6. If NO, refer to the Medical Director.*

6. Is there documented failure of oral pancreatic enzyme replacement therapy? *If YES, go to 7. If NO, refer to the Medical Director.*

7. Is the patient on prescribed enteral nutrition via tube feeding? *If YES, **approve for 6 months**. If NO, refer to the Medical Director.*

Renewal Criteria

1. Is the patient continuing enteral tube feedings? *If YES, go to 2. If NO, refer to the Medical Director.*

2. Is there documentation of no decrease in BMI while maintained on enteral feedings and Relizorb® digestive enzyme cartridge therapy? *If YES, **approve for 12 months**. If NO, refer to the Medical Director.*

Monitoring

A written plan of care has been developed for regular monitoring of signs and symptoms to detect improvement in the person's condition. Nutritional status should be monitored regularly.

CODING

Note: The Current Procedural Terminology (CPT®), Healthcare Common Procedure Coding System (HCPCS), and the 10th revision of the International Statistical Classification of Diseases and Related Health Problems (ICD-10) codes that may be listed in this policy are for reference purposes only. Listing of a code in this policy does not imply that the service is covered and there is not a guarantee of payment. Other policies and coverage guidelines may apply. When reporting services,

providers/facilities should code to the highest level of specificity using the code that was in effect on the date the service was rendered. This list may not be all inclusive.

CPT® is a registered trademark of the American Medical Association.

CPT Code	Description
N/A	

HCPCS Code	Description
B4105	In-line cartridge containing digestive enzyme(s) for enteral feeding, each

ICD-10 Codes	Description
E84.0	Cystic fibrosis with pulmonary manifestations
E84.1	Cystic fibrosis with intestinal manifestations
E84.11	Meconium ileus in cystic fibrosis
E84.19	Cystic fibrosis with other intestinal manifestations
E84.8	Cystic fibrosis with other manifestations
E84.9	Cystic fibrosis, unspecified

BENEFIT APPLICATION

Medical policies do not constitute a description of benefits. This medical necessity policy assists in the administration of the members' benefits which may vary by line of business. Applicable benefit documents govern which services/items are eligible for coverage, subject to benefit limits, or excluded completely from coverage. This policy is invoked only when the requested service is an eligible benefit as defined in the Member's applicable benefit contract on the date the service was rendered. Services determined by the Plan to be investigational or experimental, cosmetic, or not medically necessary are excluded from coverage for all lines of business.

DESCRIPTION OF SERVICES

Dosage and Administration

1. Relizorb® is intended for one time use only. At the conclusion of the feeding, discard the Relizorb®. Do not store or re-use it.

2. A single Relizorb® may be used for up to 500 mL of enteral formula. If you use less than 500 mL of enteral formula per feeding, discard the Relizorb® after use.

3. For volumes greater than 500 mL and up to 1000 mL, you can connect 2 Relizorb® cartridges together in a tandem configuration.

4. Up to 2 Relizorb® 's can be used in a day (24-hour period) and there are no requirements on the amount of time between using them.

Risk Factors/ Side Effects

Prolonged contact of the enzyme supplements with oral mucosa may cause ulcers, especially with the powdered form. To prevent this complication, children should learn to swallow capsules as early as possible; some can master the technique as young as three to four years of age. When it is necessary to open the capsules for enzyme delivery to younger children, the microspheres should be administered with food (eg, applesauce). The mouth should be inspected after eating and rinsed with water, milk, or formula if necessary to remove any beads clinging to the oral mucosa.

Other complications and considerations include:

- **Areolar excoriation for breastfeeding mothers** – In women who are breastfeeding, the areolae may become excoriated due to exposure to residual enzymes in the baby's mouth. This can be addressed by rinsing the infant's mouth after giving the enzymes and before breastfeeding.

- **Fibrosing Colonopathy** - Fibrosing colonopathy is a rare, serious adverse reaction associated with high-dose use of pancreatic enzyme replacement therapy in the trea® ent of patients with cystic fibrosis. The underlying mechanism of fibrosing colonopathy remains unknown. Patients with fibrosing colonopathy should be closely monitored because some patients may be at risk of progressing to stricture formation. Relizorb® contains lipase enzyme that is not from a porcine source. The lipase is bound to the beads, and this lipase-bead complex (iLipase) is retained within the Relizorb® cartridge. Continue to follow your physician's guidance and porcine pancreatic enzyme labeling regarding porcine pancreatic enzyme use when used in conjunction with Relizorb®.

- **Wheezing** – A few children develop wheezing from an allergic reaction if they breathe aerosolized enzyme (powder form). This can be addressed by using a microsphere form of enzyme (if possible) or by assiduous measures to avoid exposing the child to aerosolized residue.

Monitoring

A written plan of care has been developed for regular monitoring of signs and symptoms to detect improvement in the person's condition. Nutritional status should be monitored regularly.

CLINICAL EVIDENCE

Study to Evaluate Safety, Tolerability and Fat Absorption Using a Novel Enteral Feeding In-line Digestive Enzyme Cartridge (RELIZORB) in Patients with Cystic Fibrosis Receiving Enteral Feeding

The safety and efficacy of Relizorb® was assessed in a multicenter, prospective, randomized, double-blind, placebo controlled, cross-over study, conducted in 33 patients with exocrine pancreatic insufficiency (EPI) due to cystic fibrosis (CF). Patients aged 4 to 45 years with CF associated EPI, receiving supplemental enteral nutrition (EN) at least four times a week, and using PERT, were eligible for study inclusion. Exclusion criteria included uncontrolled diabetes mellitus, signs and symptoms of liver cirrhosis, portal hypertension, and significant liver disease, history of fibrosing colonopathy or recurring distal intestinal obstructive syndrome.

Thirty-three patients completed the study in the intent-to-treat population (ITT). One patient exited the study due to pulmonary exacerbation. The ITT population ranged from 5 to 34 years of age, with a mean age of 14.5 years, mean BMI (kg/m2) of 17.5 and mean weight of 41.8 (kg). Of the 33 patients, 14 were between ages 5 and 12, 16 were between ages 13 and 21, and 3 were between 22 to 34 years of age. Twenty patients were male and thirteen were female. Patients enrolled in the study had received enteral nutrition for an average of 6.6 years; the average age of initiation of enteral nutrition was approximately 8 years. Patients self-administered an average of 8-9 PERT capsules (range 2 to 21) with their overnight enteral feeding. There were 12 subjects with a diagnosis of cystic fibrosis-related diabetes (CFRD).

The absorption of fat was calculated by assessing changes in plasma concentrations over 24 hours of physiologically relevant long-chain polyunsaturated fatty acids (LCPUFAs), such as omega-3 fatty acids docosahexaenoic acid (DHA) and eicosatetraenoic acid (EPA). DHA and EPA are not only sources of energy, but are also essential components of cell membranes, and are integral in maintaining normal development and overall health. Changes in fatty acid plasma concentrations of physiologically relevant LCPUFA omega-3 fats such as DHA and EPA were assessed over 24 hours, reflecting the uptake of fat in enteral formula as a result of using Relizorb® with enteral feeding.

Results of this study indicate that Relizorb® use was safe and well tolerated with a lower frequency and severity of gastrointestinal symptoms as compared to current treatment. Relizorb® use with enteral formula also resulted in a 2.8-fold statistically significant p-value.

Background

Insufficient production of pancreatic enzymes (exocrine pancreatic insufficiency, EPI) causes malabsorption of fat, protein, and several micronutrients including the vitamins A, D, E, and K. The exact prevalence of pancreatic exocrine insufficiency is unknown. However, in patients who have chronic pancreatitis the incidence of EPI is 85% with severe disease, 30% with mild disease and 85% in newborns with cystic fibrosis. The most common causes of EPI are chronic pancreatitis and cystic fibrosis.

Cystic fibrosis causes defective functioning of the CF transmembrane conductance regulator (CFTR) which leads to impaired transport of chloride, sodium, and bicarbonate. As a result, water does not diffuse out of the cell into the mucus layer, leading to thick epithelial secretions which can lead to obstruction in the pancreatic ducts. Treatment for cystic fibrosis is pancreatic enzyme replacement therapy (PERT). PERT clearly improves fecal fat absorption in most patients with pancreatic insufficiency. CF patients have the risk of developing fibrosing colonopathy with high doses of PERT, therefore a maximum dose of 2500 lipase units/kg body weight per meal (or less than 10,000 lipase units/kg body weight per day) is recommended.

Relizorb® is a single-use, point-of-care digestive enzyme cartridge that connects in-line with existing enteral feeding pump tubing sets and patient extension sets or enteral feeding tubes. Relizorb® is designed to hydrolyze (digest) fats contained in enteral formulas, mimicking the function of the digestive enzyme lipase that is normally secreted by the pancreas, the body's digestive organ. By hydrolyzing (digesting) fats from enteral formulas, Relizorb® allows for the delivery of absorbable fatty acids and monoglycerides to patients.

Relizorb® is comprised of a clear cylindrical, plastic cartridge with a single inlet connection port and a single purple outlet connection port. The inlet and outlet ports of Relizorb® are intended to connect in-line with enteral feeding pump tubing sets and patient extension sets or enteral feeding sets. Inside the cartridge, there are small white beads. The digestive enzyme, lipase, is covalently bound to the small white beads. The lipase-bead complex, iLipase® (immobilized lipase), is retained within the cartridge during use by filters on both ends of the cartridge. The fat in enteral formulas is hydrolyzed as it comes in contact with I Lipase as the formula passes through the cartridge.

DEFINITIONS

n/a

DISCLAIMER

Approval or denial of payment does not constitute medical advice and is neither intended to guide nor influence medical decision making.

Policy Bulletins are developed by Health Partners Plans (HPP) to assist in administering plan benefits and constitute neither offers of coverage nor medical advice.

This Policy Bulletin may be updated and therefore is subject to change.

For Health Partners Plans Medicaid and Health Partners Plans CHIP products: Any requests for services that do not meet criteria set in PARP will be evaluated on a case-by-case basis.

POLICY HISTORY

This section provides a high-level summary of changes to the policy from the previous version.

Summary	Version	Version Date
2025 Annual review. References updated.	B	03/01/2024
2024 Annual review. Prior authorization updated. Age indication revised.	B	03/01/2024
New Policy	A	03/22/2023

REFERENCES

1. RELiZORB® (immobilized lipase) cartridge. www.relizorb.com. Accessed 1/5/24 https://www.relizorb.com

2. UpToDate. www.uptodate.com. Accessed 1/5/24 https://www.uptodate.com/contents/cystic-fibrosis-assessment-and-management-of-pancreatic-insufficiency?search=relizorb&source=search_result&selectedTitle=1~2&usage_type=default&display_rank=1

3. Relizorb® (Immobilized Lipase) Cartridge. Published January 2020.https://www.relizorb.com/pdf/Relizorb-Instructions-for-Use.pdf

4. **MN.018.A Medical Nutritional Support**

   MN.018.A Medical Nutritional Support.docx