# Relizorb (immobilized lipase cartridge) MNR
# Policy Number: C17943-A

**CRITERIA EFFECTIVE DATES:**

| ORIGINAL EFFECTIVE DATE | LAST REVIEWED DATE | NEXT REVIEW DUE BY OR BEFORE |
|---|---|---|
| 01/2018 | 3/17/2021 | 4/26/2022 |
| **J CODE** | **TYPE OF CRITERIA** | **LAST P&T APPROVAL/VERSION** |
| B4105 | RxPA | Q2 2021 20210428C17943-A |

**PRODUCTS AFFECTED:**
Relizorb (immobilized lipase cartridge)

**DRUG CLASS:**
Digestive Enzyme Cartridge

**ROUTE OF ADMINISTRATION:**
Enteral tube feeding

**PLACE OF SERVICE:**
Retail Pharmacy, Buy and Bill
The recommendation is that medications in this policy will be for pharmacy benefit coverage and patient self-administered

**AVAILABLE DOSAGE FORMS**:
Relizorb DEVI, NDC is 62205000020, 1 box (30 cartridges)

**FDA-APPROVED USES:**
Indicated for use in pediatric patients (ages 5 years and above) and adult patients to hydrolyze fats inenteral formula.

*The use of Enteral Feeding In-Line Cartridge (EFIC) [e.g. RELiZORB™ immobilized lipase cartridge] to deliver digestive enzymes to enteral formula is ONLY considered medically necessary for children with cystic fibrosis who receive overnight tube feedings, usually by gastrostomy with a feeding pump to help reduce early morning satiety and bloating.*

*Molina Healthcare will continue to evaluate and update this policy as relevant clinical evidence becomes available to determine whether cartridge device (e.g. RELiZORB™ immobilized lipase cartridge) to deliver digestive enzymes to enteral formula provides the safety and/or impact on health outcomes for other patient management for the use of the device*

**COMPENDIAL APPROVED OFF-LABELED USES:**
None

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**COVERAGE CRITERIA: INITIAL AUTHORIZATION**

**DIAGNOSIS:**
Exocrine pancreatic insufficiency (EPI) due to cystic fibrosis (CF)

**REQUIRED MEDICAL INFORMATION FOR ALL INDICATIONS:**
A. EXOCRINE PANCREATIC INSUFFICIENCY DUE TO CYSTICFIBROSIS:
1. Documentation of diagnosis of Cystic Fibrosis
   AND
2. (a) Documentation of diagnosis of pancreatic insufficiency with supporting laboratory evidence(fecal elastase or elevated fecal fat)
   OR
   (b) Documented strong clinical suspicion of pancreatic insufficiency: Member has two CF transmembrane conductance regulator (CFTR) variants known to be associated with pancreatic insufficiency or member has symptoms of pancreatic insufficiency (growth failure and symptoms of steatorrhea, such as diarrhea, bloating, gassiness, and abdominal pain)
   AND
3. Prescriber attests member requires enteral feedings despite optimization of pancreatic enzyme therapy(PERT) and oral nutrition support and the members body mass index (BMI) is not in the targetrange (BMI at or above the 50th percentile for age, https://www.cdc.gov/growthcharts/)
   AND
4. The member's medication history (within past 6 months) includes at least 30 days of enteral nutrition inconjunction with a trial of PERT with at least two preferred formulary digestive enzyme aids with matching indication OR documented intolerance, FDA labeled contraindication, or hypersensitivity to allpreferred formulary digestive enzyme aids with matching indication
   AND
5. The prescriber attests that there is no evidence in peer-reviewed, randomized, placebo controlled medical/scientific literature supporting the therapeutic efficacy or safety of Relizorb over current therapyand there is no evidence in peer-reviewed medical/scientific literature showing that Relizorb offers superior outcomes to established therapeutic alternatives.

**DURATION OF APPROVAL:**
Initial authorization: 6 months. Continuation of Therapy: 6 months

**QUANTITY:**
Maximum quantity of 2 cartridges per day; 2 boxes (60 cartridges) per 30 days

**PRESCRIBER REQUIREMENTS:**
Prescribed by, or in consultation with a cystic fibrosis specialist or physician from a CF center accredited by theCystic Fibrosis Foundation OR dietician. Submit consultation notes if applicable.

**AGE RESTRICTIONS:**
5 years of age and older

**CONTINUATION OF THERAPY:**
A. EXOCRINE PANCREATIC INSUFFICIENCY DUE TO CYSTICFIBROSIS:
1. Documentation of adherence to therapy at least 85% of the time as verified by prescriber and member's medication fill history (review Rx history for compliance)
   AND
2. Prescriber attests that patient has NOT experienced any toxicity related to Relizorb (immobilized lipase cartridge)

AND

3. Prescriber has provided documentation showing improvement or stabilization of members nutritionalstatus (improvement in BMI) or a decrease in symptoms of pancreatic insufficiency (steatorrhea, diarrhea, bloating, gassiness, and abdominal pain)

**CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:**

Fibrosing Colonopathy - Fibrosing colonopathy is a rare, serious adverse reaction associated with high-dose use of pancreatic enzyme replacement therapy in the treatment of patients with cystic fibrosis. The underlyingmechanism of fibrosing colonopathy remains unknown. Patients with fibrosing colonopathy should be closelymonitored because some patients may be at risk of progressing to stricture formation.

**OTHER SPECIAL CONSIDERATIONS:**

Limitations of Use: Digestive enzymes added to enteral formula via a cartridge device attached to the tubing used for enteral feeding (e.g., RELiZORB™ immobilized lipase cartridge) are considered not medically necessary for all indications, including but not limited to, patients receiving enteral tube feedings. This coverage policy is subject to change based on research and medical literature, or at the discretion of MolinaHealthcare.

**BACKGROUND:**

Alcresta Pharmaceuticals received †de novo clearance from the FDA on November 20, 2015 for RELiZORB™,as an enzyme packed cartridge. Section 510 (k) premarket approval was granted June 30, 2016. FDA concludes that this device should be classified into class II.

†De Novo FDA Classification: The FDA Modernization Act of 1997 (FDAMA) added the de novo classification option, which is also known as Evaluation of Automatic Class III Designation. This option provides an alternatepathway to classify novel devices of low-to-moderate risk. Devices that are classified through the de novo process may be marketed and used for future 510(k) submissions. Reference: FDA De Novo classification: Relizorb™. Available at: http://www.accessdata.fda.gov.

RELiZORB is designed to hydrolyze (digest) fats contained in enteral formulas. RELiZORB contains the digestive enzyme lipase bound to beads (iLipase). By hydrolyzing fats from enteral formulas, RELiZORB allows for the delivery of absorbable fatty acids and monoglycerides. Like human pancreatic lipase, the lipase inRELiZORB has sn-1, sn-3 selectivity in the hydrolysis of triglyceride fats. When enteral formula flows through RELiZORB, the lipase bound to the beads hydrolyzes fats in their triglyceride form, including important long- chain polyunsaturated fats (LCPUFAs), releasing omega-3 [docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA)] and omega-6 (linoleic acid (LA) and arachidonic acid (AA)) into their absorbable fatty acid and monoglyceride forms. The iLipase is retained within the RELiZORB cartridge by two filters as enteral formula flows through RELiZORB.

*Safety, Tolerability and Fat Absorption Using Enteral Feeding In-line Enzyme Cartridge (Relizorb) (Freedmanet al., 2017) www.clinicaltrials.gov [Trial number: NCT02598128]*
The major limitation in this study is that the study sample size is small. Only 1 feeding through digestive cartridge was, however, used to measure its effect on fat absorption, and only 7 days of digestive cartridge usewere used to measure its safety. A longer-term study is currently ongoing to assess the effects of sustained digestive cartridge use, particularly without concomitant pancreatic enzyme replacement therapy (PERT) use.

Study to Evaluate Safety, Tolerability and Fat Absorption Using a Novel Enteral Feeding In-line DigestiveEnzyme 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 a 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 ($p<0.001$) increase in DHA and EPA fatty acids. Adverse effects were noted to be headache, effecting 2/33 or (6.06%) of the participants. No limitations or caveats were noted. Absorption increased regardless of age. RELiZORB use was also associated with a greater preservation of appetite as compared to current treatment practice.

**APPENDIX:**
None

***Documentation Requirements:***
*Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.*

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**REFERENCES**


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