Effective Date: 01/2018
Last P&T Approval/Version: 04/27/2022
Next Review Due By: 04/2023
Policy Number: C17943-A

Relizorb (immobilized lipase cartridge) MNR

PRODUCTS AFFECTED

Relizorb (immobilized lipase cartridge)

COVERAGE POLICY

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.
This Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines

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

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

REQUIRED MEDICAL INFORMATION:
This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case-by case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review

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 target range (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 in conjunction 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 all preferred formulary digestive enzyme aids with matching indication

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 nutritional status (improvement in BMI) or a decrease in symptoms of pancreatic insufficiency(steatorrhea, diarrhea, bloating, gassiness, and abdominal pain)

DURATION OF APPROVAL:

Initial authorization: 6 months. Continuation of Therapy: 6 months

PRESCRIBER REQUIREMENTS:

Prescribed by, or in consultation with a cystic fibrosis specialist or physician from a CF center accredited by the Cystic Fibrosis Foundation OR dietician. Submit consultation notes if applicable.

AGE RESTRICTIONS:

5 years of age and older

QUANTITY:

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

Maximum Quantity Limits – << based on FDA label>>

PLACE OF ADMINISTRATION:

The recommendation is that medications in this policy will be for pharmacy benefit coverage and patient self-administered

DRUG INFORMATION

ROUTE OF ADMINISTRATION:

Enteral tube feeding

DRUG CLASS:

Digestive Enzyme Cartridge

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

APPENDIX

APPENDIX:
None

BACKGROUND AND OTHER CONSIDERATIONS

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 alternate pathway 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 in RELiZORB 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) (Freedman et 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 use were 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 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 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 EPAfatty 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.

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 cysticfibrosis. 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.

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 Molina Healthcare.

CODING/BILLING INFORMATION

Note: 1) This list of codes may not be all-inclusive. 2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement

HCPCS CODE	DESCRIPTION
NA	

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

REFERENCES

1. RELiZORB. RELiZORB website. http://relizorb.com/docs/pdfs/Relizorb-Instructions-forUse.pdfAccessed December 2017.
2. FDA. De Novo classification: RelizorbTM. Food and Drug Administration - Center for Devices and Radiological Health (2015). Available at: https://www.accessdata.fda.gov Accessed December 2017.
3. FDA. Premarket Approval: Relizorb™. Food and Drug Administration - Center for Devices and Radiological Health (2016). Available at: https://www.accessdata.fda.gov Accessed December 2017ClinicalTrials.gov.
4. Safety, Tolerability and Fat Absorption Using Enteral Feeding In-line Enzyme Cartridge (Relizorb),ClinicalTrials.gov Identifier: NCT02598128. Last updated: June 2016. Identifier: NCT02598128. Lastupdated: June 2016 (Final data collection date for primary outcome measure) Available at: https://clinicaltrials.gov/ct2/show/NCT02598128. Accessed December 2017.AlcrestaTherapeutics.
5. Absorption and Safety With Sustained Use of Relizorb Evaluation (ASSURE) Study in Patients With Cystic Fibrosis Receiving Enteral Feeding. Available at: www.cff.org/Trials/Finder/details/470/ASSURE-Study-of-Relizorb-in-people-with-CF-whoreceive-enteral-tube-feeding. Accessed December2017.
6. Freedman S., et al. Increased Fat Absorption from Enteral Formula Through an In-line Digestive Cartridge in Patients with Cystic Fibrosis. Journal of Pediatric Gastroenterology and Nutrition. 2017Jul;65(1):97-101. doi: 10.1097/MPG.0000000000001617. PMID: 28471913. Available at: www.ncbi.nlm.nih.gov/pubmed/?term=relizorb Accessed December2017.
7. Freedman S., et al. Options for addressing exocrine pancreatic insufficiency in patients receiving enteral nutrition supplementation. Am J Manag Care. 2017;Jul;23(12 Suppl):S220- s228. Available at:https://ajmc.s3.amazonaws.com/_media/_pdf/AJMC_A746_07_2017_ExocrinePancreaticInsufficiency Options_for_Addressing_Exocrine_Pancreatic_Insufficiency.pdf Accessed December 2017

SUMMARY OF REVIEW/REVISIONS	DATE
REVISION- Notable revisions: Required Medical Information References	Q2 2022
Q2 2022 Established tracking in new format	Historical changes on file