Original Effective Date: 01/01/2018
Current Effective Date: 06/20/2025
Last P&T Approval/Version: 04/30/2025
Next Review Due By: 04/2026
Policy Number: C12081-A

Relizorb (immobilized lipase cartridge) NC

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 cartridge device does not meet Molina Healthcare's coverage criteria and is considered not medically necessary for all indications.

The use of Enteral Feeding In-Line Cartridge (EFIC) [e.g., RELiZORB™ immobilized lipase cartridge] to deliver digestive enzymes to enteral formula is considered not medically necessary, including but not limited to, patients receiving enteral tube feedings, due to insufficient evidence in the peer-reviewed literature documenting the clinical utility and clinical validity of this type of device.

Molina Healthcare will be continuing 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 or patient management for the use of the device.

CONTINUATION OF THERAPY:
NA

DURATION OF APPROVAL:
NA

PRESCRIBER REQUIREMENTS:
NA

AGE RESTRICTIONS:
NA

QUANTITY:
NA

PLACE OF ADMINISTRATION:
NA

DRUG INFORMATION

ROUTE OF ADMINISTRATION:
Enteral tube feeding

DRUG CLASS:
Digestive Enzyme Cartridge

FDA-APPROVED USES:
Indicated for use in pediatric patients (ages 1 year and above) and adult patients to hydrolyze fats in enteral formula.

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 eicosapentaenoic acid (EPA). DHA and EPA are not only sources of energy, but are also essential components of cell membranes, andare integral in maintaining normal development and overall health. Changes in fatty acid plasmaconcentrations 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.

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:

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.

OTHER SPECIAL CONSIDERATIONS:
None

CODING/BILLING INFORMATION

CODING DISCLAIMER. *Codes listed in this policy are for reference purposes only and may not be all-inclusive or applicable for every state or line of business. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement. Listing of a service or device code in this policy does not guarantee coverage. Coverage is determined by the benefit document. Molina adheres to Current Procedural Terminology (CPT®), a registered trademark of the American Medical Association (AMA). All CPT codes and descriptions are copyrighted by the AMA; this information is included for informational purposes only. Providers and facilities are expected to utilize industry-standard coding practices for all submissions. Molina has the right to reject/deny the claim and recover claim payment(s) if it is determined it is not billed appropriately or not a covered benefit. Molina reserves the right to revise this policy as needed.*

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

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

REFERENCES

1. Alcresta Therapeutics. Relizorb: (Immobilized Lipase) Cartridge, 2017. Accessed on June 5, 2017 and available at: relizorb.com/.
2. Relizorb (immobilized lipase cartridge) [instructions for use]. Waltham, MA; Alcresta Therapeutics, Inc.: January 2025.
3. Alcresta Therapeutics. Absorption and Safety With Sustained Use of Relizorb Evaluation (ASSURE) Study in Patients With Cystic Fibrosis Receiving Enteral Feeding. Accessed on January 2020. www.cff.org/Trials/Finder/details/470/ASSURE-Study-of-Relizorb-in-people- with-CF-who-receive-enteral-tube-feeding.
4. U.S. Food and Drug Administration. Relizorb enzyme packed cartridge. 510(k) No. K163057 (traditional). Silver Spring, MD: FDA; July 12, 2017.
5. U.S. Food and Drug Administration. 510(k) Summary. K161247. Relizorb™. 2016 June 30. Accessed December 19, 2019. Available at URL address: https://www.accessdata.fda.gov/cdrh_docs/pdf16/K161247.pdf
6. ClinicalTrials.gov. Safety, Tolerability and Fat Absorption Using Enteral Feeding In-line Enzyme Cartridge (Relizorb), ClinicalTrials.gov Identifier: NCT02598128. Last updated: June 2016. Identifier: NCT02598128. Last updated: June 2016 (Final data collection date for primary outcome measure) Available at: https://clinicaltrials.gov/ct2/show/NCT02598128. Accessed January 2020.
7. 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. 2017 Jul;65(1):97-101. Doi: 10.1097/MPG.0000000000001617. PMID: 28471913. Available at: www.ncbi.nlm.nih.gov/pubmed/?term=relizorb Accessed December 2017.
8. Freedman SD, Wyatt C, Stevens J, et al. Absorption and safety with sustained use of Relizorb evaluation (ASSURE) study in patients with cystic fibrosis receiving enteral feeding. J Pediatr Gastroenterol Nutr.

2018;67(4):527-532.

SUMMARY OF REVIEW/REVISIONS	DATE
REVISION- Notable revisions: FDA-Approved Uses References	Q2 2025
REVISION- Notable revisions: FDA-Approved Uses References	Q2 2024
REVISION- Notable revisions: Required Medical Information Place of Administration Drug Class Available Dosage Forms References	Q2 2023
ANNUAL REVIEW COMPLETED- No coverage criteria changes with this annual review.	Q2 2022
Q2 2022 Established tracking in new format	Historical changes on file