CLINICAL MEDICAL POLICY	
Policy Name:	Enteral Feeding In-Line Cartridge (EFIC™)
Policy Number:	MP-054-MD-DE
Responsible Department(s):	Medical Management
Provider Notice Date:	08/15/2019; 10/15/2018; 08/01/2017
Issue Date:	09/16/2019; 11/15/2018
Effective Date:	09/16/2019; 11/15/2018; 09/01/2017
Annual Approval Date:	07/16/2020
Revision Date:	07/16/2019; 09/11/2018; 08/09/2017
Products:	Highmark Health Options Medicaid
Application:	All participating hospitals and providers
Page Number(s):	1 of 5

DISCLAIMER

Highmark Health Options medical policy is intended to serve only as a general reference resource regarding coverage for the services described. This policy does not constitute medical advice and is not intended to govern or otherwise influence medical decisions.

POLICY STATEMENT

Highmark Health Options does not provide coverage under the medical-surgical benefits of the Company's Medicaid products for medically necessary enteral feeding in-line cartridge.

This policy is designed to address medical necessity guidelines that are appropriate for the majority of individuals with a particular disease, illness or condition. Each person's unique clinical circumstances warrant individual consideration, based upon review of applicable medical records.

DEFINITIONS

Fat Malabsorption – Inadequate assimilation of dietary substances due to defects in digestion, absorption, or transport.

Lipase – A digestive enzyme that breaks down fats (triglycerides) into absorbable fatty acids and monoglycerides.

RELiZORB™ (Alcresta Therapeutics) – A single-use, point-of-care digestive enzyme cartridge device that contains an enzyme called lipase. Relizorb increases the delivery of absorbable calories from an enteral tube feeding formula by connecting the cartridge in-line with an enteral pump feed set and pump extension set. The Relizorb device is connected to the enteral tube feeding pump. The device is only for enteral feeding use and is only intended for the connection to enteral feeding lines.

De Novo FDA Classification – The Food and Drug Administration Modernization Act of 1997 (FDAMA) added the de novo classification option, which is also known as Evaluation of Automatic Class lll 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.

PROCEDURES

1. Medical Necessity Guidelines
   The use of Enteral Feeding In-Line Cartridge (EFIC) (e.g., Relizorb) with tube enteral feedings is considered experimental and investigational due to insufficient evidence in the peer-reviewed literature documenting the clinical utility and clinical validity of this type of device.

   Note: The use of Enteral Feeding In-Line Cartridge (EFIC) is considered on a case-by-case basis for members that are ages 5 years and older (under 21) with exocrine pancreatic insufficiency who are partially or completely unable to hydrolyze fats in enteral formula.

2. Post-payment Audit Statement
   The medical record must include documentation that reflects the medical necessity criteria and is subject to audit by Highmark Health Options at any time pursuant to the terms of your provider agreement.

GOVERNING BODIES APPROVAL

On July 20, 2017, Alcresta Therapeutics, Inc. received 510(k) clearance from the U.S. Food & Drug Administration (FDA) for Relizorb to be used in pediatric patients suffering from fat malabsorption.

On November 20, 2015, Alcresta Therapeutics, Inc. received de novo approval from the FDA to market Relizorb and to use Relizorb in adult patients. Relizorb is the first digestive enzyme cartridge that was created and designed to mimic the normal pancreatic function by breaking down fats in the enteral tube feeding formula.

CODING REQUIREMENTS

Non-covered Procedure Codes
All requests for the codes listed below require medical director approval

HCPCS Codes	Description
B4105	In-line cartridge containing digestive enzyme(s) for enteral feeding, each
Q9994	In-line cartridge containing digestive enzyme(s) for enteral feeding, each

Procedure codes Q9994 and B4105 will be considered on a case-by-case basis for patients age 5 to age 21 with exocrine pancreatic insufficiency-K86.81

REIMBURSEMENT

Participating facilities will be reimbursed per their Highmark Health Options contract.

SUMMARY OF LITERATURE

Fat malabsorption is a common condition in patients who cannot produce adequate digestive enzymes due to compromised pancreatic function. The condition causes a patient's gastrointestinal (GI) system to function incorrectly (NIH, 2017). Many diseases can cause malabsorption such as cystic fibrosis (CF), trauma to the pancreas, surgery to remove part of the pancreas, pancreatitis, and pancreatic cancer (BioSpace, 2016). Fat malabsorption affects many aspects of improving the health of critically ill patients, including a patient's ability to maintain or gain weight, immune system, wound healing, muscle strength, and psychological factors (Stroud, 2003). Patients with conditions that compromise pancreatic function do not produce enough pancreatic lipase necessary for fat hydrolysis (BioSpace, 2016). Individuals who have these conditions and receive enteral tube feeding may be receiving an incomplete breakdown of fats which can lead to decreased calorie intake, reduced fat digestion (e.g., omega-3 fatty acids), deficiencies of fat-soluble vitamins, and increased GI symptoms (Alcresta Therapeutics, 2017).

Due to the problems posed by fat malabsorption, there is clinical management in place which consists of enteral tube feeding. The enteral tube feeding consists of supplemental nutritional liquids that are delivered to the gastrointestinal tract through a feeding tube into the stomach or small intestine (Stroud, 2003). An enteral feeding in-line cartridge (EFIC) was designed to mimic the normal pancreatic function by breaking down fats in the enteral tube feeding formula. Breaking down the fats prior to ingestion will allow the patient who suffers from fat malabsorption to absorb more calories from omega-3 fatty acids, monoglycerides, and fat-soluble vitamins (Maki, 1993).

Currently, Relizorb is the first and only EFIC that has received de novo FDA approval for adult patients who have fat malabsorption. Relizorb is a novel in-line digestive enzyme cartridge, utilizing proprietary enzyme immobilization technology, designed for use in adult patients who receive enteral tube feeding (BioSpace, 2016). Effective October 16, 2017, the FDA classified the Enzyme Packed Cartridge into Class II (special controls) (Federal Register, 2017). The active ingredient in Relizorb is a type of lipase enzyme (iLipase™) that breaks down (hydrolysis) triglycerides into absorbable forms during enteral tube feeding (Alcresta Therapeutics, 2017).

Rationale
All EFICs are considered to be experimental and investigational to assist with fat hydrolysis (breakdown), fat absorption, and any other indications. Even with Relizorb's de novo FDA approval, there is insufficient evidence to support the safety, effectiveness, and impact on health outcomes resulting from the use of an EFIC (BioSpace, 2016). The FDA has also identified several risks associated specifically with this device, including: adverse tissue reaction, mechanical failure, reduced enzymatic effect, user error, and infection (Federal Register, 2017). There are a small number of clinical trials and evidence-based health technology assessments that have evaluated Relizorb. Hayes (2016) determined that there is insufficient evidence that assesses the patient's safety, impact on health outcomes, and patient management for the use of the Relizorb device. Hayes (2018) restated the position of insufficient evidence in a Search and Summary document for Relizorb.

Although a 33-patient clinical trial was conducted across several locations in the United States, there is a lack of human subjects on a large scale (ClinicalTrials.gov, 2016). According to Hayes (2016), the current

published clinical data for Relizorb is very small and consists of only six conference abstracts containing all pig models.

POLICY SOURCE(S)

Alcresta Therapeutics. Relizorb: (Immobilized Lipase) Cartridge, 2017. Accessed on April 5, 2017.

Alcresta Therapeutics. Alcrestra Therapeutics receives 510(K) Clearance for use of Relizorb in Children, July 20, 2017. Accessed on April 27, 2018.

Alcresta Therapeutics. Alcrestra Therapeutics receives New Innovative Technology Contract from Vizient, Inc. For Relizorb (Immobilized LIPASE) Cartridge, September 1, 2017. Accessed on April 27, 2018.

BioSpace, October 28, 2016. PRNewswire: Alcresta' Relizorb Increases Fat Absorption in Adult and Pediatric Patients with Cystic Fibrosis Receiving Enteral Nutrition. Newton, Massachusetts. Accessed on April 14, 2017.

Centers for Medicare & Medicaid Services (CMS). National Coverage Determination (NCD) for Medical Nutrition Therapy (180.1), October 1, 2002.

ClinicalTrials.gov. Safety, Tolerability and Fat Absorption Using Enteral Feeding In-line Enzyme Cartridge (Relizorb), ClinicalTrials.gov Identifier: NCT02598128. Last updated: June 2016. Accessed on April 7, 2017.

Federal Register: Food and Drug Administration (FDA). Medical Devices; Gastroenterology – Urology Devices; Classification of the Enzyme Packed Cartridge, October 16, 2017. Accessed on April 27, 2018.

Hayes, Inc. Relizorb (Alcresta Pharmaceuticals), February 4, 2016. Accessed on April 14, 2017.

Hayes, Inc. Relizorb (Alcresta Pharmaceuticals. Search & Summary, October 15, 2018. Accessed on March 18, 2019.

Maki, J., Neelagiri, M., Olshaw, B., Devarakonda, S., Loring, G. ePS05.2 Novel point of care immobilized lipase device (EFIC™) is compatible with a range of nutritional formulas and can simplify delivery of hydrolyzed fat during tube feeding, 1993. Journal of Cystic Fibrosis. Accessed on April 10, 2017.

National Institutes of Health (NIH): U.S. National Library of Medicine, 2017. MedlinePlus: Malabsorption. Bethesda, Maryland. Accessed on April 14, 2017.

Stroud, M., Duncan, H., Nightingale, J. Guidelines for enteral feeding in adult hospital patients: Institute of Human Nutrition, 2003. Accessed on April 7, 2017.

Policy History

Date	Activity
04/14/2017	Initial policy developed
06/07/2017	QI/UM Committee approval
08/03/2017	Provider effective date
08/09/2017	EHS Revisions: Added Issue Date to opening policy box; Updated Operational Guidelines.
05/01/2018	Annual Review Revisions: Added Governing Bodies updated 510(k) information; added FDA literature to Summary of Literature and Rationale; added references; added HCPCS NOC code and New 2018 HCPCS code for *In-line cartridge Enteral containing digestive enzyme(s) for enteral feeding, each;* updated operational guidelines; Added language for ages 5-21 with diagnosis of exocrine pancreatic insufficiency – Pg. 2 and Pg. 3; Added an medical director review for statement for Procedure code section on Pg. 5
09/26/2018	QI/UM Committee Review Approval
11/15/2018	Provider Effective Date
06/05/2019	Annual Review Revisions: Policy statement unchanged; Removed code B9998; Added new code B4105 due to more specificity; Updated the operational guidelines to reflect coding change in bullet one and bullet two; format changes; added new reference
07/16/2019	QI/UM Committee Review Approval
09/16/2019	Provider Effective Date