CLINICAL MEDICAL POLICY	
Policy Name:	Enteral Feeding In-Line Cartridge (EFIC™)
Policy Number:	MP-054-MD-PA
Responsible Department(s):	Medical Management
Provider Notice/Issue Date:	06/01/2023; 06/01/2022; 05/21/2021; 05/25/2020; 07/15/2019; 09/01/2018; 07/19/2017
Effective Date:	07/01/2023; 07/01/2022; 06/21/2021; 06/22/2020; 07/15/2019; 09/01/2018
Next Annual Review:	04/2024
Revision Date:	04/19/2023; 04/21/2021; 04/15/2020; 04/17/2019; 05/16/2018; 08/09/2017
Products:	Highmark Wholecare℠ Medicaid
Application:	All participating hospitals and providers
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Policy History

Date	Activity
07/01/2023	Provider Effective date
05/05/2023	PARP Approval
04/19/2023	QI/UM Committee review
04/19/2023	Annual Review: No changes to clinical criteria. Updated 'Summary of Literature' and 'Reference Sources' sections.
07/01/2022	Provider Effective date
05/09/2022	PARP approval
04/20/2022	QI/UM Committee review
04/20/2022	Annual Review: No changes to clinical criteria. Reformatted Procedures section numbering. Added the Pennsylvania TAG determination information. Updated the Summary of Literature and Reference Sources section.
06/21/2021	Provider effective date
05/07/2021	PARP approval
04/21/2021	QI/UM Committee review
04/21/2021	Annual Review: No changes to clinical criteria. Added 'EPI' to Definition section and CMS NCD information under Governing Bodies Approval section. Updated Summary of Literature and References sections.
06/22/2020	Provider effective date
05/06/2020	PARP Approval

04/15/2020	Annual Review: No change in coverage position; added definition for enteral nutrition; deleted HCPCS code Q9994 and Operational Guidelines as it was discontinued effective 1/1/2019; Updated Summary of Literature and Reference sections.
04/14/2017	Initial policy developed

Disclaimer

Highmark Wholecare℠ 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 Wholecare℠ does not provide coverage under the medical-surgical benefits of the Company's Medicaid products for medically necessary enteral feeding in-line cartridge, however coverage may be provided under specific circumstances listed below.

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.

(Current applicable Pennsylvania HealthChoices Agreement Section V. Program Requirements, B. Prior Authorization of Services, 1. General Prior Authorization Requirements.)

Definitions

Prior Authorization Review Panel (PARP) – A panel of representatives from within the Pennsylvania Department of Human Services who have been assigned organizational responsibility for the review, approval and denial of all PH-MCO Prior Authorization policies and procedures.

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. The device is an example of an enteral feeding in-line cartridge (EFIC).

Enteral Nutrition - The provision of specific nutritional requirements administered by tube feeding located in the stomach or small intestine.

Exocrine Pancreatic Insufficiency (EPI) – A condition characterized by deficiency of the exocrine pancreatic enzymes, resulting in the inability to digest food properly, or maldigestion.

Procedures

1. The use of an 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.

2. The use of an EFIC will be considered on a case-by-case basis for members that are between the ages of 5 to 21, who have been previously diagnosed with exocrine pancreatic insufficiency (EPI), and who are partially or completely unable to hydrolyze fats in enteral formula.

3. Post-payment Audit Statement
   The medical record must include documentation that reflects the medical necessity criteria and is subject to audit by Highmark Wholecare℠ 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.

The Pennsylvania Department of Human Services Technology Assessment Group (TAG) workgroup meets quarterly to discuss issues revolving around new technologies and technologies or services that were previously considered to be a program exception. During this meeting, decisions are made as to whether or not certain technologies will be covered and how they will be covered. TAG's decisions are as follow:

- Option #1: Approved - Will be added to the Fee Schedule
- Option #2: Approved as Medically Effective - Will require Program Exception
- Option #3: Approved with (or denied due to) Limited/Minimal Evidence of Effectiveness - Will require Program Exception
- Option #4: Denied - Experimental/Investigational

As of October 2019, the TAG workgroup assigned Enteral Feeding In-Line Cartridge an Option # 3, specifically for HCPCS code B4105.

Program Exception

Placement of an Enteral Feeding In-Line Cartridge device requires a program exception. The ordering physician must provide a supporting statement indicating why the requested therapy or device is medically necessary, and the alternative options have been or are likely to be ineffective, adversely affect patient compliance, or cause an adverse reaction.

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).

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).

Due to a Lack of adequate pancreatic digestive enzymes, patients with EPI experience clinical symptoms related to malabsorption of fat. Many of these patients must rely on enteral nutrition (EN) to avoid malnutrition – especially patients with acute pancreatitis and/or pancreatic cancer, children with cystic fibrosis (CF), patients in intensive care units (ICUs), patients with intestinal failure, and infants in neonatal ICUs. Hospitalization becomes necessary when malabsorption becomes malnutrition. EN must be closely managed to prevent clinical complications and practice challenges. The focus for further investigation should be on identifying all of the conditions associated with EPI (other than CF) in which EN may be indicated (eg, chronic pancreatitis, pancreatic cancer) as well as potential inpatient and intensive care

applications. Experts agreed that more population-based data would enhance current evidence. A registry function should be a top priority (Boullata, et al., 2019).

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. 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, 2017).

In a review in UpToDate (2019), the delivery system Relizorb is noted in pancreatic enzyme replacement therapy in cystic fibrosis was addressed. The information states the efficacy data is still limited, as there are small studies suggestive that the delivery system can help in early morning satiety and bloating. Additionally, there is improved fat absorption compared to baseline pancreatic enzyme replacement therapy (PERT).

EFIC for Pediatrics
Pancreatic insufficiency has been a key characteristic of cystic fibrosis (CF). CF is generally characterized as "pancreatic insufficient" (PI) or "pancreatic sufficient" (PS), based on whether the person has enough pancreatic function to grow and maintain health without supplemental pancreatic enzyme therapy (PERT). In general, about 85% of the CF population is PI early in life (before the age of 1 year). Individuals with CF born PS may become PI at any age, and without symptoms initially, emphasizing the importance of constant monitoring (Singh, Schwarzenberg, 2017).

The nutrition management for children with CF is complex. When accompanied by another severe diagnosis, optimizing growth of infants and toddlers poses an even greater challenge for parents and healthcare providers. Interventions are often maximized to prevent malnutrition and thereby minimize the risk of poor clinical outcomes. Previous studies have indicated that replacing pancreatic enzyme replacement therapy (PERT) with the digestive cartridge provided a significant therapeutic benefit to some children who were otherwise at high nutrition risk. Although the cartridge lacks protease and amylase enzymes, it has shown to be effective. Oral PERT is still required with meals and snacks containing fats and protein. With the use of the digestive cartridge, toddlers have been shown to thrive nutritionally, demonstrating weight gain, growth, and improved GI symptoms. This novel digestive cartridge is a promising therapeutic option for patients with fat malabsorption who require EN. More evidence is needed to observe its effect on long-term clinical outcomes and malnutrition (Giguere-Rich, Mathew, Reid, Autore, Guill, 2018).

Coding Requirements

Non-covered Procedure Code
All requests for the code listed below require medical director approval.

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

Reimbursement

Participating facilities will be reimbursed per their Highmark Wholecare℠ contract.

Reference Sources

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

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

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

Centers for Medicare and Medicaid Services (CMS). National Coverage Determination (NCD) for Enteral and Parenteral Nutritional Therapy (180.2). Effective Date January 1, 2022. Implementation date July 5, 2022. Accessed on March 10, 2023.

ClinicalTrials.gov. Safety, Tolerability and Fat Absorption Using Enteral Feeding In-line Enzyme Cartridge (Relizorb), ClinicalTrials.gov Identifier: NCT02598128. Last updated: January 2017. Accessed on March 22, 2021.

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, Journal of Cystic Fibrosis. 1993. Accessed on April 10, 2017.

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UpToDate. Cystic fibrosis: Assessment and management of pancreatic insufficiency. Last updated June 05, 2019 and literature review current through February 2020. Accessed on April 1, 2020.

Boullata JI, Clarke JL, Stone A, Skoufalos A, Nash DB. Optimizing Clinical and Cost Outcomes for Patients on Enteral Nutrition Support for Treatment of Exocrine Pancreatic Insufficiency: Proceedings from an Expert Advisory Board Meeting. Popul Health Manag. June 2019. Accessed on March 22, 2021.

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Giguere-Rich C, Mathew A, Reid E, Autore K, Guill MF. American Society for Parenteral and Enteral Nutrition. Use of an In-line Digestive Cartridge With Enteral Nutrition Improves the Weight Trajectory of 2 Children With Cystic Fibrosis Complicated by Another Medical Diagnosis. Nutrition in Clinical Practice Volume 33 Number 2. April 2018. Accessed on March 17, 2022.

Department of Health and Human Services. Technology Assessment Group (TAG) Coverage Decisions. Managed Care Operations Memorandum: General Operations: MCOPS Memo # #08/2019-011. Accessed on March 17, 2022.