Clinical Policy: Pancrelipase (Creon, Pancreaze, Pertzye, Viokace, Zenpep)

Reference Number: CP.PCH.44
Effective Date: 03.01.22
Last Review Date: 02.22
Line of Business: Commercial, HIM

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Pancrelipase is a combination of porcine-derived lipases, proteases, and amylases.

FDA Approved Indication(s)

- Pancrelipase (Creon®) is indicated for the treatment of exocrine pancreatic insufficiency due to cystic fibrosis, chronic pancreatitis, pancreatectomy, or other conditions.
- Pancrelipase (Pancreaze®, Pertzye®, Zenpep®) is indicated for the treatment of exocrine pancreatic insufficiency due to cystic fibrosis or other conditions.
- Pancrelipase (Viokace®), in combination with a proton pump inhibitor, is indicated in adults for the treatment of exocrine pancreatic insufficiency due to chronic pancreatitis or pancreatectomy.

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Creon, Pancreaze, Pertzye, Viokace, and Zenpep are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Pancreatic Insufficiency (must meet all)**:**

1. Diagnosis of exocrine pancreatic insufficiency;
2. If request is for Pertzye, Viokace or Pancreaze: failure of Creon and Zenpep, unless both are contraindicated or clinically significant adverse effects are experienced;
3. If request is for Viokace, both of the following (a and b):
   a. Age ≥ 18 years;
   b. Viokace is prescribed concurrently with a proton pump inhibitor;
4. Dose does not exceed 2,500 lipase units/kg/meal or 4,000 lipase units/g of fat ingested per day.

Approval duration:
HIM – 6 months
Commercial – 12 months or duration of request, whichever is less

B. Other diagnoses/indications

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is

NOT authorized): CP.CPA.09 for commercial and HIM.PA.154 for health insurance marketplace.

II. Continued Therapy

A. Pancreatic Insufficiency (must meet all)**:**

1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed 2,500 lipase units/kg/meal or 4,000 lipase units/g of fat ingested per day.

Approval duration:
HIM – 12 months
Commercial – 12 months or duration of request, whichever is less

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 12 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial and HIM.PA.154 for health insurance marketplace.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off-label use policies – CP.CPA.09 for commercial and HIM.PA.154 for health insurance marketplace or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
FDA: Food and Drug Administration

Appendix B: Therapeutic Alternatives
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug*	Dosing Regimen	Dose Limit/ Maximum Dose
Creon® (pancrelipase)	*Infants (up to 12 months)* • 3,000 lipase units (1 capsule) per 120 mL of formula or per breast-feeding. Do not mix capsule contents directly into formula or breast milk prior to administration. *Children > 12 Months and < 4 Years*	Dosing should not exceed the recommended maximum dosage set forth

Drug*	Dosing Regimen	Dose Limit/ Maximum Dose
	• Begin with 1,000 lipase units/kg of body weight per meal to a maximum of 2,500 lipase units/kg of body weight per meal (or ≤ 10,000 lipase units/kg of body weight per day), or < 4,000 lipase units/g fat ingested per day. *Children ≥ 4 years and Adults ≥ 18 years* • Begin with 500 lipase units/kg of body weight per meal to a maximum of 2,500 lipase units/kg of body weight per meal (or ≤ 10,000 lipase units/kg of body weight per day), or < 4,000 lipase units/g fat ingested per day.	by the Cystic Fibrosis Foundation Consensus Conferences Guidelines: 2,500 lipase units/kg/meal or 4,000 lipase units/g of fat ingested per day
Zenpep® (pancrelipase)	*Infants (up to 12 months)* • 3,000 lipase units (1 capsule) per 120 mL of formula or per breast-feeding. Do not mix capsule contents directly into formula or breast milk prior to administration. *Children > 12 Months and < 4 Years* • Begin with 1,000 lipase units/kg of body weight per meal to a maximum of 2,500 lipase units/kg of body weight per meal (or ≤ 10,000 lipase units/kg of body weight per day), or < 4,000 lipase units/g fat ingested per day. *Children ≥ 4 years and Adults ≥ 18 years* • Begin with 500 lipase units/kg of body weight per meal to a maximum of 2,500 lipase units/kg of body weight per meal (or ≤ 10,000 lipase units/kg of body weight per day), or < 4,000 lipase units/g fat ingested per day.	

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.
**Each agent is not interchangeable with any other pancrelipase product*

Appendix C: Contraindications/Boxed Warnings
None reported

V. Dosage and Administration

Drug Name*	Dosing Regimen	Maximum Dose
Creon® (pancrelipase)	*Infants (up to 12 months)* • 3,000 lipase units (1 capsule) per 120 mL of formula or per breast-feeding. Do not mix capsule contents directly into formula or breast milk prior to administration. *Children > 12 Months and < 4 Years*	Dosing should not exceed the recommended maximum dosage set forth

Drug Name*	Dosing Regimen	Maximum Dose
	• Begin with 1,000 lipase units/kg of body weight per meal to a maximum of 2,500 lipase units/kg of body weight per meal (or ≤ 10,000 lipase units/kg of body weight per day), or < 4,000 lipase units/g fat ingested per day. *Children ≥ 4 years and Adults ≥ 18 years* Begin with 500 lipase units/kg of body weight per meal to a maximum of 2,500 lipase units/kg of body weight per meal (or ≤ 10,000 lipase units/kg of body weight per day), or < 4,000 lipase units/g fat ingested per day.	by the Cystic Fibrosis Foundation Consensus Conferences Guidelines: 2,500 lipase units/kg/meal or 4,000 lipase units/g of fat
Pancreaze® (pancrelipase)	*Infants (up to 12 months)* • 2,600 lipase units (1 capsule) per 120 mL of formula or per breast-feeding. Do not mix capsule contents directly into formula or breast milk prior to administration. *Children > 12 Months and < 4 Years* • Begin with 1,000 lipase units/kg of body weight per meal to a maximum of 2,500 lipase units/kg of body weight per meal (or ≤ 10,000 lipase units/kg of body weight per day), or < 4,000 lipase units/g fat ingested per day. *Children ≥ 4 years and Adults ≥ 18 years* Begin with 500 lipase units/kg of body weight per meal to a maximum of 2,500 lipase units/kg of body weight per meal (or ≤ 10,000 lipase units/kg of body weight per day), or < 4,000 lipase units/g fat ingested per day.	
Pertzye (pancrelipase)	*Infants (up to 12 months)* • 4,000 lipase units (1 capsule) per 120 mL of formula or per breast-feeding. Do not mix capsule contents directly into formula or breast milk prior to administration. *Children > 12 Months and < 4 Years* • Begin with 1,000 lipase units/kg of body weight per meal to a maximum of 2,500 lipase units/kg of body weight per meal (or ≤ 10,000 lipase units/kg of body weight per day), or < 4,000 lipase units/g fat ingested per day. *Children ≥ 4 years and Adults ≥ 18 years* • Begin with 500 lipase units/kg of body weight per meal to a maximum of 2,500 lipase units/kg of body weight per meal (or ≤ 10,000 lipase units/kg of body weight per day), or < 4,000 lipase units/g fat ingested per day.	
Viokace (pancrelipase)	*Adults ≥ 18 years*	

Drug Name*	Dosing Regimen	Maximum Dose
	Begin with 500 lipase units/kg of body weight per meal to a maximum of 2,500 lipase units/kg of body weight per meal (or ≤ 10,000 lipase units/kg of body weight per day), or < 4,000 lipase units/g fat ingested per day.	
Zenpep (pancrelipase)	*Infants (up to 12 months)* • 3,000 lipase units (1 capsule) per 120 mL of formula or per breast-feeding. Do not mix capsule contents directly into formula or breast milk prior to administration. *Children > 12 Months and < 4 Years* • Begin with 1,000 lipase units/kg of body weight per meal to a maximum of 2,500 lipase units/kg of body weight per meal (or ≤ 10,000 lipase units/kg of body weight per day), or < 4,000 lipase units/g fat ingested per day. *Children ≥ 4 years and Adults ≥ 18 years* • Begin with 500 lipase units/kg of body weight per meal to a maximum of 2,500 lipase units/kg of body weight per meal (or ≤ 10,000 lipase units/kg of body weight per day), or < 4,000 lipase units/g fat ingested per day.	

**Each agent is not interchangeable with any other pancrelipase product*

VI. Product Availability

Drug Name	Availability
Creon® (pancrelipase)	Delayed-release capsules: • 3,000 USP units of lipase; 9,500 USP units of protease; 15,000 USP units of amylase • 6,000 USP units of lipase; 19,000 USP units of protease; 30,000 USP units of amylase 12,000 USP units of lipase; 38,000 USP units of protease; 60,000 USP units of amylase • 24,000 USP units of lipase; 76,000 USP units of protease; 120,000 USP units of amylase • 36,000 USP units of lipase; 114,00 USP units of protease; 180,000 USP units of amylase
Pancreaze® (pancrelipase)	Capsules: • 2,600 USP units of lipase; 8,800 USP units of protease; 15,200 USP units of amylase • 4,200 USP units of lipase; 14,200 USP units of protease; 24,600 USP units of amylase • 10,500 USP units of lipase; 35,500 USP units of protease; 61,500 USP units of amylase

Drug Name	Availability
	• 16,800 USP units of lipase; 56,800 USP units of protease; 98,400 USP units of amylase • 21,000 USP units of lipase; 54,700 USP units of protease; 83,900 USP units of amylase • 37,000 USP units of lipase; 93,300 USP units of protease; 149,900 USP units of amylase
Pertzye (pancrelipase)	Delayed-release capsules: • 4,000 USP units of lipase; 14,375 USP units of protease; 15,125 USP units of amylase • 8,000 USP units of lipase; 28,750 USP units of protease; 30,250 USP units of amylase • 16,000 USP units of lipase; 57,500 USP units of protease; 60,500 USP units of amylase • 24,000 USP units of lipase; 86,250 USP units of protease; 90,750 USP units of amylase
Viokace (pancrelipase)	Tablets: • 10,440 USP units of lipase; 39,150 USP units of protease; 39,150 USP units of amylase • 20,880 USP units of lipase; 78,300 USP units of protease; 78,300 USP units of amylase
Zenpep (pancrelipase)	Capsules: • 3,000 USP units of lipase; 10,000 USP units of protease; 14,000 USP units of amylase capsules have a white opaque cap and white opaque body, red imprint with “APTALIS 3” • 5,000 USP units of lipase; 17,000 USP units of protease; 24,000 USP units of amylase capsules have a white opaque cap and white opaque body, blue imprint with “APTALIS 5” • 10,000 USP units of lipase; 32,000 USP units of protease; 42,000 USP units of amylase capsules have a yellow opaque cap and white opaque body, blue imprint with “APTALIS 10” • 15,000 USP units of lipase; 47,000 USP units of protease; 63,000 USP units of amylase capsules have a red opaque cap and white opaque body, blue imprint with “APTALIS 15” • 20,000 USP units of lipase; 63,000 USP units of protease; 84,000 USP units of amylase capsules have a green opaque cap and white opaque body, blue imprint with “APTALIS 20” • 25,000 USP units of lipase; 79,000 USP units of protease; 105,000 USP units of amylase capsules have a blue opaque cap and white opaque body, blue imprint with “APTALIS 25” • 40,000 USP units of lipase; 126,000 USP units of protease; 168,000 USP units of amylase capsules have an orange opaque cap and white opaque body, blue imprint with “APTALIS 40”

VII. References

1. Creon Prescribing Information. North Chicago, IL: AbbVie Inc.; March 2020. Available at: https://www.creon.com/. Accessed March 9, 2021.
2. Pancreaze Prescribing Information. Campbell, CA: VIVUS, Inc.; March 2020. Available at: https://pancreaze.com/. Accessed March 9, 2021.
3. Pertzye Prescribing Information. Bethlehem, PA: Digestive Care, Inc.; March 2020. Available at: https://resources.chiesiusa.com/Pertzye/PERTZYE_PI.pdf. Accessed August 4, 2020.
4. Viokace Prescribing Information. Irvine, CA: Allergan, Inc.; March 2020. Available at: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=d85c7e20-4e1d-43cd-a64b-ced3bda70eed. Accessed August 4, 2020.
5. Zenpep Prescribing Information. Irvine, CA: Allergan, Inc.; March 2020. Available at: https://www.zenpep.com. Accessed August 4, 2020.
6. Cystic Fibrosis Foundation. Pancreatic enzymes clinical care guidelines: executive summary. Available at: https://www.cff.org/Care/Clinical-Care-Guidelines/Nutrition-and-GI-Clinical-Care-Guidelines/Pancreatic-Enzymes-Clinical-Care-Guidelines/. Accessed December 11, 2019.
7. Borowitz DS, Grant RJ Durie PR, the Consensus Committee. Use of pancreatic enzyme supplements for patients with cystic fibrosis in the context of fibrosing colonopathy. J Pediatr. 1995; 127:681-84.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created based on CP.PMN.226 and HIM.PA.155, previously approved clinical guidance, and March SDC decision to create policy for Commercial and HIM LOB in the event that auto PA requests get rejected at POS (intended to limit non FDA-indicated utilization); redirections revised from Creon and Pancreaze to Creon and Zenpep per SDC direction in October; revised approval duration for Commercial line of business from length of benefit to 12 months or duration of request, whichever is less.	10.29.21	02.22

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.