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

Reference Number: CP.PCH.44
Effective Date: 03.01.22
Last Review Date: 11.23
Line of Business: Commercial, HIM

Revision Log

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

Description

Pancrelipase (Creon®, Pancreaze®, Pertzye®, Viokace®, Zenpep®) is a combination of porcine-derived lipases, proteases, and amylases.

FDA Approved Indication(s)

Creon, Pancreaze, Pertzye, and Zenpep are indicated for the treatment of exocrine pancreatic insufficiency in adult and pediatric patients.

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 or Viokace: Failure of Pancreaze, Creon, and Zenpep, unless clinically significant adverse effects are experienced or all are contraindicated;
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 one of the following (a, b, or c):
   a. 2,500 lipase units/kg per meal;
   b. 10,000 lipase units/kg per day;
   c. 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 (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial and HIM.PA.33 for health insurance marketplace; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial and HIM.PA.103 for health insurance marketplace; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial and HIM.PA.154 for health insurance marketplace.

II. Continued Therapy

A. Pancreatic Insufficiency (must meet all)**:**
1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed one of the following (a, b, or c):
   a. 2,500 lipase units/kg per meal;
   b. 10,000 lipase units/kg per day;
   c. 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. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial and HIM.PA.33 for health insurance marketplace; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial and HIM.PA.103 for health insurance marketplace; or

2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: 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
Not applicable

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* • 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. Adult patients with chronic pancreatitis or pancreatectomy may require an initial starting dosage of 1,000 lipase units/kg of body weight per meal.	2,500 lipase units/kg/meal, 10,000 lipase units/kg/day, or 4,000 lipase units/g of fat ingested/day Higher dosages may be administered if documented effective by fecal fat measures or improvement of malabsorption
Pancreaze (pancrelipase)	*Infants (up to 12 months)*	

Drug Name*	Dosing Regimen	Maximum Dose
	• 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* 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.	

Drug Name*	Dosing Regimen	Maximum Dose
	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)	Delayed-release 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 • 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

Drug Name	Availability
	• 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)	Delayed-release 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" • 60,000 USP units of lipase; 189,600 USP units of protease; 252,600 USP units of amylase. Capsules have a powder blue opaque cap with two black stripes and white opaque body, printed with "APTALIS 60"

VII. References

1. Creon Prescribing Information. North Chicago, IL: AbbVie Inc.; February 2024. Available at: https://www.creon.com/. Accessed March 6, 2024.
2. Pancreaze Prescribing Information. Campbell, CA: VIVUS, Inc.; February 2024. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/022523s019lbl.pdf. Accessed March 6, 2024.

3. Pertzye Prescribing Information. Bethlehem, PA: Digestive Care, Inc.; February 2024. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/022175s010lbl.pdf. Accessed March 6, 2024.
4. Viokace Prescribing Information. Irvine, CA: Allergan, Inc.; February 2024. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/022542s009lbl.pdf. Accessed March 6, 2024.
5. Zenpep Prescribing Information. Irvine, CA: Allergan, Inc.; February 2024. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/022210s026lbl.pdf. Accessed March 6, 2024.
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 July 18, 2023.
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
4Q 2022 annual review: no significant changes; clarified dosing by separating various dosing options; modified Pancreaze as delayed release capsules per updated prescribing information; reference reviewed and updated. Template changes applied to other diagnoses/indications and continued therapy section.	07.11.22	11.22
Per November SDC: for Pancrease removed redirection to of Creon and Zenpep; for Pertzye and Viokace requests added Pancreaze as required step through drug in addition to Creon and Zenpep.	11.18.22	02.23
4Q 2023 annual review: no significant changes; references reviewed and updated.	06.29.23	11.23
RT4: for Zenpep added new 60,000 USP unit strength.	12.05.23	
RT4: updated the FDA Approved Indication(s) section to reflect generalization of the approved indication language for Creon, Pancreaze, Pertzye, and Zenpep; revised maximum dose criterion to include 10,000 lipase units/kg per day per PI; updated maximum dosing in Section V per revised FDA labels for all products.	03.06.24	

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.