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Clinical Guideline

Guideline Number: PG027, Ver. 4

Pancreatic Digestive Enzymes - pancrelipase (Brand Names: Creon; Pancreaze; Pertzye; Viokace; Zenpep)

Disclaimer

Clinical guidelines are developed and adopted to establish evidence-based clinical criteria for utilization management decisions. Clinical guidelines are applicable according to policy and plan type. The Plan may delegate utilization management decisions of certain services to third parties who may develop and adopt their own clinical criteria.

Coverage of services is subject to the terms, conditions, and limitations of a member's policy, as well as applicable state and federal law. Clinical guidelines are also subject to in-force criteria such as the Centers for Medicare & Medicaid Services (CMS) national coverage determination (NCD) or local coverage determination (LCD) for Medicare Advantage plans. Please refer to the member's policy documents (e.g., Certificate/Evidence of Coverage, Schedule of Benefits, Plan Formulary) or contact the Plan to confirm coverage.

Summary

The pancreas is an organ located in the abdomen. It has two main functions: it releases hormones (insulin and glucagon) to help regulate blood sugar. It also produces enzymes that help digest and convert the food we eat into energy for the body's functions.

Digestive enzymes produced by the pancreas enter the small intestine and break down fats, starch, and protein from food. Exocrine pancreatic insufficiency (EPI) occurs when pancreatic enzymes are not produced, resulting in maldigestion or the ability to digest food properly. Patients with EPI experience broad symptoms such as abdominal discomfort, bloating, cramping, increased flatulence, nutritional and vitamin deficiency, weight loss, and diarrhea or steatorrhea. Edema (swelling), anemia (low red blood cell count), osteopenia (loss of bone mass) or osteomalacia (softening of bones), and certain neurologic disorders may result from severe nutritional deficiencies.

EPI can be caused by chronic pancreatitis, cystic fibrosis, previous pancreatic surgery, blockage of pancreatic duct, Shwachman-Diamond syndrome (a rare genetic condition), and other disorders of the digestive tract. EPI is treated with dietary adjustments, vitamin supplementation (primarily the fat-soluble vitamins A, D, E, and K), and pancreatic enzyme replacement therapy (PERT) which is the mainstay of treatment for EPI. If abdominal symptoms do not improve with PERT, alternate causes of symptoms should be evaluated and treated.

PERT products all contain porcine-derived amylases, lipases, and proteases. The formulations available in the US are categorized as enteric-coated (Creon, Pancreaze, Pertzye, and Zenpep) and non-enteric coated (Viokace). Enteric coating prevents the enzymes from being denatured by gastric acid as the coating dissolves in the duodenum. The PERT products are not interchangeable due to their different enzyme contents and release mechanisms. New prescriptions will be needed when switching between products.

The choice of PERT products will depend on indications. The prescribed dose should be individualized and adjusted based on the patient's weight, fat content of the diet, severity of steatorrhea, and clinical symptoms. The total daily PERT dose should reflect food consumption of approximately three meals plus two or three snacks per day. Half of the prescribed dose is usually for snacks. The initial dose is generally 500 lipase units/kg/meal orally. Dosing is increased to a maximum of 2500 lipase units/kg/meal, 4000 lipase units/g fat ingested/day, or 10,000 lipase units/kg/day. Higher doses should be used with caution and only if they are documented to be effective by 3-day fecal fat measurements that indicate a significantly improved fat absorption.

Adverse effects of PERT which have been reported include fibrosing colonopathy at high doses, abdominal discomfort, flatulence, biliary tract stones, pruritus, and allergic reactions.

The efficacy of PERT is determined by the timing of doses. Pancrelipase should be taken with meals and snacks . Improvement in symptoms is reflected by stool consistency and weight gain. The most common reasons for treatment failure include inadequate dosage or inadequate amount of enzymes that reach the duodenum. Changing to another formulation may improve symptoms if the patient is still having inadequate responses after increasing dose, timing PERT with food intake, acid suppression, and lifestyle changes that avoid risk factors for the underlying causes of EPI.

Pertzye is the only product that has G-tube administration information in the package insert; however instructions are available for G-tube administration with other products.

Table 1: Product Label Information

Product	Formulation	FDA-Approved Indications and Usage
CREON (pancrelipase) delayed-release capsules	Enteric-coated capsule	Treatment of exocrine pancreatic insufficiency due to cystic fibrosis (FDA approved in infants, children, adolescents, and adults), chronic pancreatitis, pancreatectomy, or other conditions (FDA approved in adults).
PANCREAZE ® (pancrelipase) delayed-release capsules	Enteric-coated capsule	Treatment of exocrine pancreatic insufficiency due to cystic fibrosis or other conditions (FDA approved in infants, children, adolescents, and adults).
PERTZYE (pancrelipase) delayed-release capsules	Enteric-coated with bicarbonate	
ZENPEP® (pancrelipase) delayed release capsules	Enteric-coated capsule	
VIOKACE® (pancrelipase) tablets	Non–enteric-coated tablet	Treatment of exocrine pancreatic insufficiency due to chronic pancreatitis or pancreatectomy in combination with a proton pump inhibitor (FDA approved in adults). NOTE: Since VIOKACE is not enteric-coated, it should be taken in combination with a proton pump inhibitor

NOTE: Pancrelipase products are not interchangeable. All of these products contain a combination of porcine-derived lipases, proteases, and amylases.

Definitions

"Chronic pancreatitis" is inflammation of the pancreas that does not heal or improve. It may get worse over time and lead to permanent damage. Chronic pancreatitis eventually impairs a patient's ability to digest food and make pancreatic hormones.

"Exocrine pancreatic insufficiency" is a condition which occurs when the pancreas does not make enough of a specific enzyme the body uses to digest food in the small intestine.

"Fibrosing colonopathy" is a disease that arises in people with cystic fibrosis treated with high doses of pancreatic enzyme supplements. Signs and symptoms include thickening of the bowel wall, abdominal pain, abdominal swelling, vomiting, and constipation.

"Hyperuricemia" is an excess of uric acid in the blood.

"Pruritus" is an uncomfortable, irritating, or itchy sensation.

"Steatorrhea**"** is the result of fat malabsorption and is characterized by pale, bulky, and malodorous stools. These stools often float on top of the toilet water with oily droplets and are difficult to flush.

Medical Necessity Criteria for Initial Authorization

The Plan considers pancrelipase (Brand Names: Creon; Pancreaze; Pertzye; Viokace; Zenpep) medically necessary when ALL the following criteria are met:

1. The requested product is prescribed by or in consultation with a gastroenterologist; ***AND***
2. The requested product is for the treatment of exocrine pancreatic insufficiency caused by ONE of the following:
    a. Cystic fibrosis**; *or***
    b. Chronic pancreatitis**; *or***
    c. Pancreatectomy**; *or***
    d. GI bypass surgery (e.g., Billroth II gastroenterostomy)**; *or***
    e. other conditions in which pancreatic insufficiency impairs fat digestion; ***AND***
3. Chart documentation and laboratory test results (such as fecal elastase measurement, ultrasound, secretin pancreatic function test) indicate exocrine pancreatic insufficiency due to one of the diagnoses listed above; ***AND***
4. Clinical chart documentation indicates the member has been provided individualized dietary advice OR will be referred to a nutritionist; ***AND***
5. The request meets ONE of the following:
    a. The requested product is Creon, or Zenpep**; *or***
    b. The requested product is Viokace, and documentation is provided that Viokace will be used with a proton pump inhibitor**; *or***

c. The requested product is for Pancreaze or Pertzye, AND the member is unable to use or has tried and failed ALL of the following:
    i. Creon***; and***
    ii. Zenpep***; and***
    iii. Viokace

If the above prior authorization criteria are met, then the pancrelipase product will be approved for 12 months.

Medical Necessity Criteria for Reauthorization:

Reauthorization for 12 months will be granted if BOTH of the following are met:

1. the member still meets the applicable initial criteria; and
2. recent chart documentation (within the past 12 months) shows that the patient is experiencing relief in maldigestion-related symptoms (e.g., relief in symptoms of abdominal pain, steatorrhea, and/or flatulence).

Experimental or Investigational / Not Medically Necessary

pancrelipase (Brand Names: Creon; Pancreaze; Pertzye; Viokace; Zenpep) for any other indication is considered not medically necessary by the Plan, as this is deemed to be experimental, investigational, or unproven. Additionally, the safety and efficacy of Viokace in patients younger than 18 years of age has not been established.

References

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Clinical Guideline Revision / History Information

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