

Indiana Medicaid Therapeutics Committee **Therapeutic Class Review Summary**

Therapeutic Class: Pancreatic Enzymes

Overview:

The USP defines standards for two pancreatic enzyme preparations, pancreatin and pancrelipase, which are porcine derived enzymes containing amylase, lipase, and protease. Pancreatin contains not less than 2 USP units of lipase activity, not less than 25 USP units of amylase activity, and not less than 25 USP units of protease activity. Pancrelipase contains not less than 24 USP units of lipase activity, not less than 100 USP units of amylase activity, and not less than 100 USP units of protease activity. Following activation in the alkaline pH of the duodenum, pancrelipase and pancreatin release high levels of lipase, amylase, and protease, which facilitate the hydrolysis of fats into glycerol and fatty acids, starches into dextrans and sugars, and proteins into peptides. Factors that influence the effectiveness of pancrelipase and pancreatin are those that affect the quantity of enzymatic activity reaching the small intestine, such as dose, gastrointestinal pH, and the microsphere size of the product. Doses of pancreatic enzymes must be individualized according to patient need and response, but should not exceed the recommended maximum dosage set forth by the Cystic Fibrosis Foundation Consensus Conferences Guidelines.

Pancreatic enzyme replacement therapy is indicated in patients with deficient exocrine pancreatic secretions, such as in cystic fibrosis (CF), chronic pancreatitis, post-pancreatectomy, ductal obstructions caused by cancer of the pancreas or common bile duct, pancreatic insufficiency, and for steatorrhea of malabsorption syndrome and postgastrectomy. Currently, more than 30 different pancrelipase formulations are marketed in the United States, with varying concentrations of amylase, lipase, and protease. There are no pancreatin products available at this time. Many pancreatic enzyme products have been available since before the Food, Drug, and Cosmetic Act of 1938. In April 1995, the US Food and Drug Administration (FDA) decided that manufacturers of over-the-counter (OTC) pancreatic enzyme products must have FDA approval before marketing, and that these products would be approved as prescription only agents. In April 2004, the FDA notified manufacturers of pancreatic enzyme products that they must have approval via the submission of a new drug application (NDA) within the next four years in order to remain on the US market. This decision was made after the FDA reviewed data that showed variations in the effectiveness and manufacturing quality of the currently marketed pancreatic extract drug products, which might significantly affect efficacy, and potentially

lead to over- or under-dosing. Recently, Creon[®] became the first pancreatic enzyme product to receive FDA approval under the new guidelines for this class. Zenpep[®] and Pancreaze[®] have also received FDA approval and are now available.

Brand Name	Lipase / Protease / Amylase	Manufacturer
Creon [®]	6,000 / 19,000 / 30,000	Solvay
Creon [®]	12,000 / 38,000 / 60,000	
Creon [®]	24,000 / 76,000 / 120,000	
Pancreaze [®]	4,200/10,000/17,500	Ortho McNeil Janssen
Pancreaze [®]	10,500/25,000/43,750	
Pancreaze [®]	16,800/40,000/70,000	
Pancreaze [®]	21,000/37,000/61,000	
Pancrelipase	5,000 / 17,000 / 27,000	X-Gen
Zenpep [®]	5,000 / 17,000 / 27,000	Eurand
Zenpep [®]	10,000 / 34,000 / 55,000	
Zenpep [®]	15,000 / 51,000 / 82,000	
Zenpep [®]	20,000 / 68,000 / 109,000	

Summary:

Pancreatic enzyme replacement therapy is indicated in patients with deficient exocrine pancreatic secretions, such as in cystic fibrosis, chronic pancreatitis, post-pancreatectomy, ductal obstructions caused by cancer of the pancreas or common bile duct, pancreatic insufficiency, and for steatorrhea of malabsorption syndrome and postgastrectomy. Currently, more than 30 different pancrelipase formulations are marketed in the United States, with varying concentrations of amylase, lipase, and protease. Unfortunately, there is a lack of robust clinical trial data available to evaluate and compare these products. In April 2004, the FDA notified manufacturers of pancreatic enzyme products that they must have approval via the submission of an NDA within the next four years in order to remain on the US market. As a result, the only products currently on the market that have received FDA approval are Creon[®], Zenpep[®], and Pancreaze[®].