



## **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 dextrins 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<sup>®</sup> became the first pancreatic enzyme product to receive FDA approval under the new guidelines for this class. Zenpep<sup>®</sup> has also received FDA approval and is now available. Other pancreatic enzyme products including Ultrase and Pancrecarb have NDA applications that have been submitted to the FDA but have not yet received formal approval. Many other pancreatic enzyme products continue to be available because of their established use as replacement therapy to treat serious conditions including chronic pancreatitis and CF.



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<b>Brand Name</b>	<b>Lipase / Protease / Amylase</b>	<b>Manufacturer</b>
Creon <sup>®</sup>	6,000 / 19,000 / 30,000	Solvay
Creon <sup>®</sup>	12,000 / 38,000 / 60,000	
Creon <sup>®</sup>	24,000 / 76,000 / 120,000	
Dygase <sup>™</sup>	2,400 / 30,000 / 30,000	Cypres
Lipram <sup>®</sup> 4500	4,500 / 25,000 / 20,000	Global
Lipram <sup>®</sup> CR 5	5,000 / 18,750 / 16,600	
Lipram <sup>®</sup> PN 10	10,000 / 30,000 / 30,000	
Lipram <sup>®</sup> PN 16	16,000 / 48,000 / 48,000	
Lipram <sup>®</sup> PN 20	20,000 / 44,000 / 56,000	
Lipram <sup>®</sup> UL 20	20,000 / 65,000 / 65,000	
Palcaps <sup>®</sup> 10	10,000 / 37,500 / 33,200	
Palcaps <sup>®</sup> 20	20,000 / 75,000 / 66,400	
Pancrease <sup>®</sup> MT 4	4,000 / 12,000 / 12,000	Ortho-McNeil
Pancrease <sup>®</sup> MT 10	10,000 / 30,000 / 30,000	
Pancrease <sup>®</sup> MT 16	16,000 / 48,000 / 48,000	
Pancrease <sup>®</sup> MT 20	20,000 / 44,000 / 56,000	
Pancrecarb <sup>®</sup> MS 4	4,000 / 25,000 / 25,000	Digestive Care
Pancrecarb <sup>®</sup> MS 8	8,000 / 45,000 / 40,000	
Pancrecarb <sup>®</sup> MS 16	16,000 / 52,000 / 52,000	
Panocaps <sup>®</sup> 4500	4,500 / 25,000 / 20,000	Breckenridge
Panocaps <sup>®</sup> MT 16	16,000 / 48,000 / 48,000	
Panocaps <sup>®</sup> MT 20	20,000 / 44,000 / 56,000	
Panokase <sup>®</sup>	8,000 / 30,000 / 30,000	Breckenridge
Panokase <sup>®</sup> 16	16,000 / 60,000 / 60,000	
Ultracaps <sup>®</sup> MT 20	20,000 / 65,000 / 65,000	Breckenridge
Ultrase <sup>®</sup>	4,500 / 25,000 / 20,000	Axcand Scandipharm
Ultrase <sup>®</sup> MT 12	12,000 / 39,000 / 39,000	
Ultrase <sup>®</sup> MT 18	18,000 / 58,500 / 58,500	
Ultrase <sup>®</sup> MT 20	20,000 / 65,000 / 65,000	
Viokase <sup>®</sup> 8	8,000 / 30,000 / 30,000	Axcand Scandipharm
Viokase <sup>®</sup> 16	16,000 / 60,000 / 60,000	
Zenpep <sup>®</sup>	5,000 / 17,000 / 27,000	Eurand
Zenpep <sup>®</sup>	10,000 / 34,000 / 55,000	
Zenpep <sup>®</sup>	15,000 / 51,000 / 82,000	
Zenpep <sup>®</sup>	20,000 / 68,000 / 109,000	



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## **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, many products have been discontinued, and it is unclear how many agents will continue to be available for use. To date, only Creon<sup>®</sup> and Zenpep<sup>®</sup> have received FDA approval.