TABLE 371-8 FDA-APPROVED PANCREATIC ENZYME (PANCRELIPASE) PREPARATIONS

	Enzyme Content/Unit Dose, U.S. Pharmacopeia Units		
Product	**Lipase[a]**	**Amylase[a]**	**Protease[a]**
Immediate-Release Capsule			
Non-enteric-coated			
Viokace 10,440	10,440	391,550	39,150
Viokace 20,880	20,880	78,300	78,300
Delayed-Release Capsules			
Enteric-coated mini-microspheres			
Creon 3000	3000	15,000	9500
Creon 6000	6000	30,000	19,000
Creon 12,000	12,000	60,000	38,000
Creon 24,000	24,000	120,000	76,000
Enteric-Coated Mini-Tablets			
Ultresa 13,800	13,800	27,600	27,600
Ultresa 20,700	20,700	41,400	41,400
Ultresa 23,000	23,000	46,000	46,000
Enteric-Coated Beads			
Zenpep 3000	3000	16,000	10,000
Zenpep 5000	5000	27,000	17,000
Zenpep 10,000	10,000	55,000	34,000
Zenpep 15,000	15,000	82,000	51,000
Zenpep 20,000	20,000	109,000	68,000
Zenpep 25,000	25,000	136,000	85,000
Enteric-Coated Micro-Tablets			
Pancreaze 4200	4200	17,500	10,000
Pancreaze 10,500	10,500	43,750	25,000
Pancreaze 16,800	16,800	70,000	40,000
Pancreaze 21,000	21,000	61,000	37,000
Bicarbonate-Buffered Enteric-Coated Microspheres			
Pertzye 8000	8000	30,250	28,750
Pertzye 16,000	16,000	60,500	57,500

[a]U.S. Pharmacopeia (USP) units per tablet or capsule

Note: The FDA has mandated all enzyme manufacturers to submit New Drug Applications (NDAs) for all pancreatic extract drug products after reviewing data that showed substantial variations among currently marketed products. Numerous manufacturers have investigations under way to seek FDA approval for the treatment of exocrine pancreatic insufficiency due to cystic fibrosis or other conditions under the new guidelines for this class of drugs (*www.fda.gov*).

80,000–100,000 units of lipase taken during the meal may be necessary to normalize nutritional parameters in malnourished chronic pancreatitis patients, and some may require acid suppression with proton pump inhibitors.

ABDOMINAL PAIN

The management of pain in patients with chronic pancreatitis is problematic.

Recent meta-analyses have shown no consistent benefit of *enzyme therapy* at reducing pain in chronic pancreatitis. In some patients with idiopathic chronic pancreatitis, conventional non-enteric-coated enzyme preparations containing high concentrations of serine proteases may relieve mild abdominal pain or discomfort. The pain relief experienced by these patients actually may be due to improvements in the dyspepsia from maldigestion.

Gastroparesis is also quite common in patients with chronic pancreatitis. It is important to recognize and treat with prokinetic drugs because treatment with enzymes may fail simply because gastric dysmotility is interfering with the delivery of enzymes into the upper intestine. A recent prospective study reported that pregabalin can improve pain in chronic pancreatitis and lower pain medication requirement.

Endoscopic treatment of chronic pancreatitis pain may involve sphincterotomy, stenting, stone extraction, and drainage of a pancreatic pseudocyst. Therapy directed to the pancreatic duct would seem to be most appropriate in the setting of a dominant stricture, especially if a ductal stone has led to obstruction. The use of endoscopic stenting for patients with chronic pain, but without a dominant stricture, has not been subjected to any controlled trials. It is now appreciated that significant complications can occur from stenting (i.e., bleeding, cholangitis, stent migration, pancreatitis, and stent clogging). In patients with large-duct disease usually from alcohol-induced chronic pancreatitis, ductal decompression with *surgical therapy* has been the therapy of choice. Among such patients, 80% seem to obtain immediate relief; however, at the end of 3 years, one-half of the patients have recurrence of pain. Two randomized prospective trials comparing endoscopic to surgical therapy for chronic pancreatitis demonstrated that surgical therapy was superior to endoscopy at decreasing pain and improving quality of life in selected patients with dilated ducts and abdominal pain. This would suggest that chronic pancreatitis patients with dilated ducts and pain should be considered for surgical intervention. The role of preoperative stenting prior to surgery as a predictor of response has yet to be proven.

A Whipple procedure, total pancreatectomy, and autologous islet cell transplantation have been used in selected patients with chronic pancreatitis and abdominal pain refractory to conventional therapy. The patients who have benefited the most from total pancreatectomy have chronic pancreatitis without prior pancreatic surgery or evidence of islet cell insufficiency. The role of this procedure remains to be fully defined but may be an option in lieu of ductal decompression surgery or pancreatic resection in patients with intractable, painful small-duct disease, particularly as the standard surgical procedures tend to decrease islet cell yield. Celiac plexus block has not resulted in long-lasting pain relief.

HEREDITARY PANCREATITIS

Hereditary pancreatitis is a rare disease that is similar to chronic pancreatitis except for an early age of onset and evidence of hereditary factors. A genomewide search using genetic linkage analysis identified the hereditary pancreatitis gene on chromosome 7. Mutations in ion codons 29 (exon 2) and 122 (exon 3) of the cationic trypsinogen gene cause autosomal dominant forms of hereditary pancreatitis. The codon 122 mutations lead to a substitution of the corresponding arginine with another amino acid, usually histidine. This substitution, when it occurs, eliminates a fail-safe trypsin self-destruction site necessary to eliminate trypsin that is prematurely activated within the acinar cell. These patients have recurring attacks of severe abdominal pain that may last from a few days to a few weeks. The serum amylase and lipase levels may be elevated during acute attacks but are usually normal. Patients frequently develop pancreatic calcification, diabetes mellitus, and steatorrhea; in addition, they have an increased incidence of pancreatic carcinoma, with the cumulative incidence being as high as 40% by age 70 years. A recent natural history study of hereditary pancreatitis in more than 200 patients from France reported that abdominal pain started in childhood at age 10 years, steatorrhea developed at age 29 years, diabetes at age 38 years, and pancreatic carcinoma at age 55 years. Such patients often require surgical ductal decompression for pain relief. Abdominal complaints in relatives of patients with hereditary pancreatitis should raise the question of pancreatic disease.

PSTI, or SPINK1, is a 56-amino-acid peptide that specifically inhibits trypsin by physically blocking its active site. SPINK1 acts as the first line of defense against prematurely activated trypsinogen in the acinar cell. Recently, it has been shown that the frequency of SPINK1 mutations in patients with idiopathic chronic pancreatitis is markedly increased, suggesting that these mutations may be associated with pancreatitis.

PANCREATIC ENDOCRINE TUMORS

Pancreatic endocrine tumors are discussed in Chap. 113.