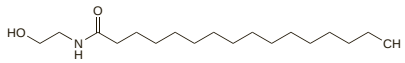
Palmidrol *(rINN)*

Palmidrolum. *N*-(2-Hydroxyethyl)palmitamide.

Пальмидрол

$C_{18}H_{37}NO_2$ = 299.5.

CAS — 544-31-0.



Profile

Palmidrol is a naturally occurring lipid compound that may be isolated from soybean lecithin, egg-yolk, or peanut meal. It has been used as an immunostimulant. It is given orally in doses of 1 g two or three times daily for the treatment of respiratory-tract infections.

Preparations

Proprietary Preparations (details are given in Part 3)
Chile: Palmitan†.

Pancreatic Enzymes

Pancreatin *(BAN)*

Haimajauhe (pancreas powder); Kasos milteliai (pancreas powder); Pancréas, poudre de (pancreas powder); Pancreatina; Pancreatinum; Pancreatis pulvis (pancreas powder); Pankreaspulver (pancreas powder); Pankreatiini; Pankreatin; Pankreáz-por (pancreas powder).

CAS — 8049-47-6.

Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), *Jpn*, and *US* as pancreatin or another pancreatic exocrine extract or both.

Ph. Eur. 6.2 (Pancreas Powder; Pancreatis Pulvis; Pancreatic Extract BP 2008). It is prepared from the fresh or frozen pancreases of mammals. It contains various enzymes having proteolytic, lipolytic, and amylolytic activities. Each mg of pancreas powder contains not less than 1 Ph. Eur. unit of total proteolytic activity, not less than 15 Ph. Eur. units of lipolytic activity, and not less than 12 Ph. Eur. units of amylolytic activity. A slightly brown, amorphous powder. Partly soluble in water; practically insoluble in alcohol. Store in airtight containers.

BP 2008 (Pancreatin). A preparation of mammalian pancreas containing enzymes having protease, lipase, and amylase activity. Each mg of pancreatin contains not less than 1.4 FIP units of free protease activity, not less than 20 FIP units of lipase activity, and not less than 24 FIP units of amylase activity. It may contain sodium chloride. A white or buff amorphous powder, free from unpleasant odour. Soluble or partly soluble in water forming a slightly turbid solution; practically insoluble in alcohol and in ether. Store at a temperature not exceeding 15°.

USP 31 (Pancreatin). A substance containing enzymes, principally amylase, lipase, and protease, obtained from the pancreas of the hog or of the ox. It is a cream-coloured, amorphous powder, having a faint, characteristic, but not offensive odour. Its greatest activities are in neutral or faintly alkaline media; more than traces of mineral acids or large amounts of alkali hydroxides make it inert. An excess of alkali carbonate also inhibits its action.

Pancreatin contains, in each mg, not less than 25 USP units of amylase activity, not less than 2 USP units of lipase activity, and not less than 25 USP units of protease activity. Pancreatin of a higher digestive power may be labelled as a whole-number multiple of the 3 minimum activities, or may be diluted with lactose, or with sucrose containing not more than 3.25% of starch, or with pancreatin of lower digestive power. Store in airtight containers at a temperature not exceeding 30°.

Pancrelipase *(USAN)*

Pancrelipasa.

CAS — 53608-75-6.

Pharmacopoeias. In *US*.

USP 31 (Pancrelipase). A substance containing enzymes, principally lipase, with amylase and protease, obtained from the pancreas of the hog. It is a cream-coloured, amorphous powder having a faint characteristic, but not offensive odour. Its greatest activities are in neutral or faintly alkaline media; more than traces of mineral acids or large amounts of alkali hydroxides make it inert. An excess of alkali carbonate also inhibits its action. Pancrelipase contains, in each mg, 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. Store in airtight containers preferably at a temperature not exceeding 25°.

Units

The Ph. Eur. and USP units of protease activity depend upon the rate of hydrolysis of casein, those of lipase activity depend upon the rate of hydrolysis of olive oil, and those of amylase activity depend upon the rate of hydrolysis of starch. Because of differences in the assay conditions, the Ph. Eur. and USP units are not readily comparable.

FIP units of protease, lipase, and amylase activity are approximately equivalent to Ph. Eur. units.

Adverse Effects and Precautions

Pancreatic enzyme supplements commonly cause gastrointestinal adverse effects such as abdominal discomfort and nausea and vomiting. They may also cause buccal and perianal irritation, particularly in infants. Colonic strictures (fibrosing colonopathy) have occurred, mainly in children with cystic fibrosis receiving high doses of pancreatin preparations; the use of high doses in patients with cystic fibrosis should preferably be avoided (see Effects on the Gastrointestinal Tract, below). Adequate hydration should be maintained at all times in patients receiving higher strength preparations.

Hypersensitivity reactions have been reported; these may be sneezing, lachrymation, or skin rashes. Hyperuricaemia or hyperuricosuria have occurred with high doses. There have been occasional reports of the contamination of pancreatin preparations with *Salmonella* spp.

Effects on folic acid. Pancreatic extract significantly inhibited folate absorption in healthy subjects and in pancreatic insufficient patients.[1] Testing *in vitro* showed that pancreatic extract formed insoluble complexes with folate. It was suggested[1] that patients being treated for pancreatic insufficiency should be monitored for folate status or given folic acid supplementation, particularly if pancreatic enzymes and bicarbonate (or cimetidine) were being used together in the treatment regimen.

1. Russell RM, *et al*. Impairment of folic acid absorption by oral pancreatic extracts. *Dig Dis Sci* 1980; **25:** 369–73.

Effects on the gastrointestinal tract. ***FIBROSING COLONOPATHY.*** After the introduction of high-strength pancreatic enzyme preparations, there were a number of reports[1-6] of colonic strictures in children with cystic fibrosis who received these formulations, and the problem, now dubbed fibrosing colonopathy, was reviewed.[7,8] Fibrosing colonopathy has also been reported[9] in an adult who was not thought to have cystic fibrosis, but who had been taking high doses of pancreatic enzyme supplements, including 2 with methylacrylic acid copolymer (MAC) coatings, for 5 years after surgical removal of the pancreas.

The pathogenesis and aetiology of this condition still remain unclear. Dose-related thickening of the colon wall has been described,[10] and an inflammatory or immune-mediated mechanism has been suggested.[11,12] It has also been suggested that the type of preparation used may have a role. An analysis[13] of cases of fibrosing colonopathy occurring in the UK between 1984 and 1994 demonstrated that there was a dose-related association between the high-strength preparations and this adverse effect although there was some criticism and debate surrounding the methodology of this particular analysis.[14-16] A subsequent case-control study[17] of patients in the US presenting between 1990 and 1994 concluded that there was a strong association between high daily doses of pancreatic enzymes, in any form, and the development of fibrosing colonopathy; no significant differences were observed between the various high- and low-strength preparations used. Re-analysis[18] of the UK data found a highly statistically significant association with the intake of preparations using MAC for enteric coating, but no evidence that a high intake of lipase in the absence of MAC was a risk factor for the disease. However, at least one case has been reported with a preparation that did not contain this material.[19]

As a result of these problems, high-strength preparations were withdrawn in the USA, while in the UK, the CSM recommended[20] that unless special reasons exist, patients with cystic fibrosis should not use high-strength pancreatin preparations, and that all patients treated with these products should be monitored carefully for gastrointestinal obstruction. The CSM later elaborated on these recommendations:[21] they advised that *Nutrizym 22*, *Pancrease HL*, and *Panzytrat 25 000* [now discontinued in the UK] should not be used in children with cystic fibrosis who were aged 15 years or less; that the total daily dose of pancreatic enzyme supplements for patients with cystic fibrosis should not exceed a lipase activity of 10 000 units/kg; and that patients on any pancreatin preparation should be reviewed to exclude colonic damage if new abdominal symptoms or a change in symptoms occurred. Other risk factors identified were male sex, more severe cystic fibrosis, and the concomitant use of laxatives.[21] The US Cystic Fibrosis Foundation has made recommendations for the management of patients who do not respond adequately to moderate doses of pancreatic enzymes,[22] and similar recommendations have been made in the UK.[23]

1. Smyth RL, *et al.* Strictures of ascending colon in cystic fibrosis and high-strength pancreatic enzymes. *Lancet* 1994; **343:** 85–6.
2. Oades PJ, *et al.* High-strength pancreatic enzyme supplements and large-bowel stricture in cystic fibrosis. *Lancet* 1994; **343:** 109.
3. Campbell CA, *et al.* High-strength pancreatic enzyme supplements and large-bowel stricture in cystic fibrosis. *Lancet* 1994; **343:** 109–110.
4. Mahony MJ, Corcoran M. High-strength pancreatic enzymes. *Lancet* 1994; **343:** 599–600.
5. Knabe N, *et al.* Extensive pathological changes of the colon in cystic fibrosis and high-strength pancreatic enzymes. *Lancet* 1994; **343:** 1230.
6. Pettei MJ, *et al.* Pancolonic disease in cystic fibrosis and high-dose pancreatic enzyme therapy. *J Pediatr* 1994; **125:** 587–9.
7. Taylor CJ. Colonic strictures in cystic fibrosis. *Lancet* 1994; **343:** 615–16. Correction. *ibid.*; 1108.
8. Taylor CJ. The problems with high dose pancreatic enzyme preparations. *Drug Safety* 1994; **11:** 75–9.
9. Bansi DS, *et al.* Fibrosing colonopathy in an adult owing to over use of pancreatic enzyme supplements. *Gut* 2000; **46:** 283–5.
10. MacSweeney EJ, *et al.* Relationship of thickening of colon wall to pancreatic-enzyme treatment in cystic fibrosis. *Lancet* 1995; **345:** 752–6.
11. Croft NM, *et al.* Gut inflammation in children with cystic fibrosis on high-dose enzyme supplements. *Lancet* 1995; **346:** 1265–7.
12. Lee J, *et al.* Is fibrosing colonopathy an immune mediated disease? *Arch Dis Child* 1997; **77:** 66–70.
13. Smyth RL, *et al.* Fibrosing colonopathy in cystic fibrosis: results of a case-control study. *Lancet* 1995; **346:** 1247–51.
14. Dodge JA. Concern about records of fibrosing colonopathy study. *Lancet* 2001; **357:** 1526–7.
15. Dodge JA. Further comments on fibrosing colonopathy study. *Lancet* 2001; **358:** 1546.
16. O'Hara D, Talbot IC. Further comments on fibrosing colonopathy study. *Lancet* 2001; **358:** 1546.
17. FitzSimmons SC, *et al.* High-dose pancreatic-enzyme supplements and fibrosing colonopathy in children with cystic fibrosis. *N Engl J Med* 1997; **336:** 1283–9.
18. Prescott P, Bakowski MT. Pathogenesis of fibrosing colonopathy: the role of methacrylic acid copolymer. *Pharmacoepidemiol Drug Safety* 1999; **8:** 377–84.
19. Taylor CJ, Steiner GM. Fibrosing colonopathy in a child on low-dose pancreatin. *Lancet* 1995; **345:** 1106–7.
20. Committee on Safety of Medicines/Medicines Control Agency. Update: bowel strictures and high-potency pancreatins. *Current Problems* 1994; **20:** 13. Available at: http://www.mhra.gov.uk/home/idcplg?IdcService=GET_FILE&dDocName=CON2015632&RevisionSelectionMethod=LatestReleased (accessed 06/08/08)
21. Committee on Safety of Medicines/Medicines Control Agency. Fibrosing colonopathy associated with pancreatic enzymes. *Current Problems* 1995; **21:** 11. Available at: http://www.mhra.gov.uk/Publications/Safetyguidance/CurrentProblemsinPharmacovigilance/CON2023217 (accessed 06/08/08)
22. Borowitz DS, *et al.* Use of pancreatic enzyme supplements for patients with cystic fibrosis in the context of fibrosing colonopathy. *J Pediatr* 1995; **127:** 681–4.
23. Littlewood JM. Fibrosing colonopathy in cystic fibrosis: commentary, implications of the Committee on Safety of Medicines 10 000 IU lipase/kg/day recommendation for use of pancreatic enzymes in cystic fibrosis. *Arch Dis Child* 1996; **74:** 466–8.

MOUTH ULCERATION. In 3 children taking preparations of pancreatic extracts (*Pancrex V powder*, *Pancrex V Forte*), severe mouth ulceration and angular stomatitis, causing dysphagia, loss of weight, and pyrexia, were attributed to digestion of the mucous membrane due to retention of the preparations in the mouth before swallowing.[1]

1. Darby CW. Pancreatic extracts. *BMJ* 1970; **2:** 299–300.

Hypersensitivity. A successful desensitisation regimen has been described[1] for a child with cystic fibrosis who vomited within 1 to 2 hours after ingestion of pancreatic enzymes, suggestive of a type I hypersensitivity reaction.

1. Chamarthy LM, *et al.* Desensitization to pancreatic enzyme intolerance in a child with cystic fibrosis. Abstract: *Pediatrics* 1998; **102:** 134–5. Full version: http://pediatrics.aappublications.org/cgi/reprint/102/1/e13.pdf (accessed 14/07/06)

Uses and Administration

Pancreatic enzymes (as pancreatin or pancrelipase) hydrolyse fats to glycerol and fatty acids, break down protein into peptides, proteoses and derived substances, and convert starch into dextrins and sugars. They are given by mouth in conditions of pancreatic exocrine deficiency such as pancreatitis and cystic fibrosis. They are available in the form of powder, capsules containing powder or enteric-coated granules (which may be opened before use and the contents sprinkled on soft food), enteric-coated tablets, or granules. If pancreatic enzymes are mixed with liquids or food the resulting mixture should not be allowed to stand for more than 1 hour before use. Histamine H_2-receptor antagonists, such as cimetidine or ranitidine, have been given an hour before a dose in an attempt to lessen destruction of the pancreatic enzymes by gastric acid, or proton pump inhibitors such as omeprazole may be used; alternatively, antacids may be given with the dose.

The dose of pancreatic enzymes is adjusted according to the needs of the individual patient and will also depend on the dosage form. In the UK, proprietary preparations generally provide about 5 000 to 10 000 units of lipase activity per dose-unit and usual doses, given with each meal, range from about 5 000 to 56 000 units of lipase activity (with varying proportions of protease and amylase activity, depending on the preparation). In the USA, doses providing up to 40 000 USP units of lipase activity may be given with each meal. So-called high-strength or high-potency preparations are available for those receiving high doses, and typically contain about 20 000 to 40 000 units of lipase activity per dose unit, but their use has been associated with the development of fibrosing colonopathy in children with cystic fibrosis (see Effects on the Gastrointestinal Tract, above). Such preparations are consequently not recommended for children in the UK and authorities there consider the total daily dose of pancreatic supplements for patients with cystic fibrosis should not exceed a lipase activity of 10 000 units/kg.

Purified lipase preparations have also been used. A recombinant human bile-salt stimulated lipase is under investigation for the treatment of fat malabsorption in patients with exocrine pancreatic insufficiency and cystic fibrosis.

Pancreatin is also used to remove protein deposits from the surface of soft contact lenses (p.1622).

Cystic fibrosis. Patients with cystic fibrosis (p.166) suffer from pancreatic insufficiency and consequent malabsorption. Pancreatin or pancrelipase may therefore play a role in the management of the disorder, being taken before or with each meal or snack.

Generic substitution. Three patients with cystic fibrosis whose gastrointestinal symptoms had been well controlled with pancrelipase developed symptoms after substitution of generic pancrelipase for their previous brand.[1] The generic product had a different lipase content and was almost inactive at stomach pH *in vitro*, apparently because of a defective enteric coating. Different brands of pancrelipase may not be therapeutically equivalent and should not be routinely substituted.

1. Hendeles L, *et al.* Treatment failure after substitution of generic pancrelipase capsules: correlation with in vitro lipase activity. *JAMA* 1990; **263:** 2459–61.

Pancreatitis. Pancreatitis is an inflammatory process affecting the pancreas. Acute pancreatitis comprises necrosis of pancreatic tissue occurring in an otherwise healthy gland, whereas chronic pancreatitis is the manifestation of pathological processes resulting in inflammation and progressive fibrosis of pancreatic tissue. Acute disease may be superimposed on a background of chronic pancreatitis.

Acute pancreatitis is frequently associated with either biliary-tract disorders (such as gallstones or cholecystitis) or the intake of large amounts of alcohol, or less frequently with abdominal surgery, pancreatic trauma, hyperparathyroidism, hyperlipidaemia, infection, or the adverse effects of drugs. Endoscopic retrograde cholangiopancreatography (ERCP) is followed by acute pancreatitis in anywhere between 3 and 40% of patients,[1] although it may also be used successfully to treat acute pancreatitis associated with gallstones.[2]

Symptoms of acute pancreatitis include pain, which ranges from mild to extremely severe and which typically persists for several days, nausea and vomiting, ileus, and hypovolaemic shock. In severe disease, pulmonary, renal, and hepatic failure, encephalopathy, and death may ensue. A mortality rate of about 10% has been reported.

The management of acute disease is essentially supportive.[1,3-8] Adequate analgesia for pain is important (see Pancreatic Pain, p.9); in mild cases, analgesia, adequate hydration, and temporary interruption of oral intake of food to 'rest' the pancreas may be adequate. In more severe disease enteral or parenteral nutrition may be needed,[1,7] although some[5,6,8] advocate enteral over parenteral nutrition because of potential complications with the latter. Since most patients suffer from hypoxaemia it has been recommended that they should receive additional humidified oxygen by mask, with mechanical ventilation if blood gases indicate the development of severe pulmonary failure. Shock should be managed with blood or plasma, and electrolyte solutions, while insulin may be required for disturbances of glucose homoeostasis.

The value of other interventions is mostly doubtful. As an extension of the concept of 'pancreatic rest', inhibitors of pancreatic secretion including somatostatin or octreotide have been tried but without significant effect, while protease inhibitors such as aprotinin or gabexate mesilate have also proven disappointing,[3] perhaps because activation of pancreatic proteases (thought to play a significant role in pathogenesis) has already taken place by the time therapy is begun.[3] A meta-analysis[9] of studies using aprotinin or gabexate mesilate suggested that these might reduce mortality in moderate to severe acute pancreatitis. However, this conclusion has been criticised[10] based on weaknesses in the original studies and the criteria used for severity grading. Gabexate and somatostatin may have roles in the prevention of acute pancreatitis after ERCP,[11] but it remains difficult to identify which patients should be offered prophylaxis, since not all will develop the condition.[1,3] Furthermore, it has been suggested[12] that with improved techniques, the use of prolonged infusions of pharmacological prophylaxis against severe pancreatitis after ERCP may no longer be justified. Preliminary studies of the platelet-activating factor antagonist lexipafant for treatment of pancreatitis were initially promising but were not supported by subsequent larger studies.[4]

Although prophylactic antibacterials are often given, there has been some uncertainty about their value (see p.183). In a review[13] of the treatment of acute necrotising pancreatitis, it was pointed out that early studies that failed to show any benefit of prophylactic antibacterials had also included patients with interstitial oedematous acute pancreatitis. The authors emphasised that the prevention of infection is critical in acute necrotising pancreatitis, since the development of infected necrosis substantially increases mortality, and concluded that use of antibacterials is the mainstay of management in such patients. Some[6] do not recommend antibacterial prophylaxis in patients with necrotising pancreatitis; for others,[8] accepted treatment is to start intravenous imipenem or meropenem for 14 days when infection is suspected but to stop it rapidly if not confirmed, although this view was challenged.[14] A systematic review[15] found that antibacterial prophylaxis appeared to be associated with significantly decreased mortality in patients with pancreatic necrosis but there was no significant reduction in the rates of infected pancreatic necrosis. It is also possible that beta lactams might be preferable to quinolone plus imidazole regimens, although no firm conclusions could be drawn because of small sample size. Further better designed studies are needed to support antibacterial prophylaxis and, should these prove beneficial, to compare beta lactams with quinolones directly.

The role of surgery continues to be somewhat controversial; it is accepted for complications or when a potential surgical emergency exists.[1,3,5-8] Surgery to remove the gallbladder is usually delayed in severe episodes of acute, gallstone-related pancreatitis to allow resolution of the inflammatory process and improvement in the patient's nutritional state.[1] Early ERCP to clear an obstructed bile duct may reduce complications in patients with predicted severe pancreatitis, but does not reduce mortality.[2]

Chronic pancreatitis is frequently associated with high alcohol-intake although a tropical form,[1] associated with malnutrition, also exists, and some cases are idiopathic[16] or auto-immune.[17] Symptoms include recurrent episodes of pain (often less excruciating and of shorter duration than in acute pancreatitis) which normally become less severe and frequent over the years with the inexorable progression of fibrosis. Loss of exocrine tissue eventually leads in many patients to pancreatic exocrine insufficiency, with maldigestion and steatorrhoea, and in some to diabetes mellitus due to islet cell loss. Other symptoms may include cholestatic jaundice, fatty degeneration of the liver, stenosis of the bile duct, and hepatic cirrhosis (although this may also be due to alcohol intake). It has been estimated that more than 50% of patients die within 20 years of diagnosis, with those who continue to drink alcohol being at greatest risk. In some patients, chronic pancreatitis is a premalignant disorder.[1]

Adequate analgesia with opioids is essential (see Pancreatic Pain, p.9). Nerve blocks of the coeliac plexus with phenol or alcohol have generally proved disappointing, although coeliac plexus blocks using corticosteroids and local anaesthetic may be effective.[1] However, response to nerve ablation procedures is often limited and of short duration.[16] Patients should be advised to abstain from alcohol, which can exacerbate the frequency and severity of painful episodes.[1] A low-fat diet is also recommended, or for patients who cannot tolerate oral intake, parenteral or enteral nutrition.[16] Steatorrhoea requires replacement of pancreatic enzymes with preparations of pancreatin or pancrelipase. Because the enzymes are inactivated by gastric acid they may be taken after inhibitors of acid secretion[1] or with a sodium-containing antacid such as sodium bicarbonate (magnesium-, calcium-, and possibly aluminium-containing antacids may further interfere with fat absorption). Alternatively, enteric-coated enzyme preparations may be used.[16] In some patients with mild disease pancreatic enzyme replacement may also improve pain, although for this purpose only non-enteric coated preparations are effective.[16] Supplements of fat-soluble vitamins are not normally necessary, but may be given intravenously if required. Diabetes should be managed appropriately once steatorrhoea is under control.

Surgery, up to and including total pancreatectomy, has an important role in the relief of intractable pain, and may also be necessary for the management of complications.[1,16] Endoscopic decompression using contrast media containing prednisolone and ulinastatin has been reported to produce beneficial responses.[18] Anecdotal results suggest that some patients with pancreatic pseudocysts, which usually require surgical drainage, may respond to octreotide.[19]

1. Mitchell RMS, *et al.* Pancreatitis. *Lancet* 2003; **361:** 1447–55.
2. Ayub K, *et al.* Endoscopic retrograde cholangiopancreatography in gallstone-associated acute pancreatitis. Available in The Cochrane Database of Systematic Reviews; Issue 3. Chichester: John Wiley; 2004 (accessed 09/03/06).
3. Norton ID, Clain JE. Optimising outcomes in acute pancreatitis. *Drugs* 2001; **61:** 1581–91.
4. Nam JH, Murthy S. Acute pancreatitis—the current status in management. *Expert Opin Pharmacother* 2003; **4:** 235–41.
5. Working Party of the British Society of Gastroenterology, Association of Surgeons of Great Britain and Ireland, Pancreatic Society of Great Britain and Ireland, and Association of Upper GI Surgeons of Great Britain and Ireland. UK guidelines for the management of acute pancreatitis. *Gut* 2005; **54** (suppl III): iii1–iii9. Also available at: http://gut.bmj.com/cgi/reprint/54/suppl_3/iii1.pdf (accessed 06/08/08)
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7. Whitcomb DC. Acute pancreatitis. *N Engl J Med* 2006; **354:** 2142–50.
8. Frossard J-L, *et al.* Acute pancreatitis. *Lancet* 2008; **371:** 143–52.
9. Seta T, *et al.* Treatment of acute pancreatitis with protease inhibitors: a meta-analysis. *Eur J Gastroenterol Hepatol* 2004; **16:** 1287–93.
10. Singh VP, Chari ST. Protease inhibitors in acute pancreatitis: lessons from the bench and failed clinical trials. *Gastroenterology* 2005; **128:** 2172–4.
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12. Whitcomb DC. Acute pancreatitis. *N Engl J Med* 2006; **355:** 961.
13. Baron TH, Morgan DE. Acute necrotizing pancreatitis. *N Engl J Med* 1999; **340:** 1412–17. Correction. *ibid.*; **341:** 460.
14. Cullimore J, *et al.* Antibiotics in acute necrotising pancreatitis. *Lancet* 2008; **371:** 1072.
15. Villatoro E, *et al.* Antibiotic therapy for prophylaxis against infection of pancreatic necrosis in acute pancreatitis. Available in The Cochrane Database of Systematic Reviews; Issue 4. Chichester: John Wiley; 2006 (accessed 06/06/08).
16. Callery MP, Freedman SD. A 21-year-old man with chronic pancreatitis. *JAMA* 2008; **299:** 1588–94.
17. Finkelberg DL, *et al.* Autoimmune pancreatitis. *N Engl J Med* 2006; **355:** 2670–6.
18. Ohwada M, *et al.* New endoscopic treatment for chronic pancreatitis, using contrast media containing ulinastatin and prednisolone. *J Gastroenterol* 1997; **32:** 216–21.
19. Gullo L, Barbara L. Treatment of pancreatic pseudocysts with octreotide. *Lancet* 1991; **338:** 540–1.

Preparations

BP 2008: Gastro-resistant Pancreatin Tablets; Pancreatin Granules; ***USP 31:*** Pancreatin Tablets; Pancrelipase Capsules; Pancrelipase Delayed-release Capsules; Pancrelipase Tablets.

Proprietary Preparations (details are given in Part 3)

Arg.: Creon; Pancrecura†; Pankreozym; Prolipase; ***Austral.:*** Bioglan Panazyme; Cotazym S Forte; Creon; Opti-Free Enzymatic†; Opti-Plus†; Pancrease; Panzytrat; Polyzym†; ***Austria:*** Kreon; Pancrin; Pankreon forte; Panzynorm; ***Belg.:*** Creon; Pancrease†; ***Braz.:*** Cotazym; Creon; Opti-Free Enzimatica†; Opti-Free Supraclens; Pancrease; Panzytrat; Polyzym; ***Canad.:*** Cotazym; Creon; Opti-Zyme†; Pancrease; Ultrase; Viokase; ***Chile:*** Creon; ***Cz.:*** Gastrix; Kreon; Pancreolan; Pangrol; Panzynorm; Panzytrat; ***Denm.:*** Creon; Pancrease; Pankreon†; ***Fin.:*** Creon; Pancrease; Pankreon†; ***Fr.:*** Creon; Licrease†; Polyzym†; ***Ger.:*** Bilipeptal Mono; Carzodelan†; Cholspasminase N; Cotazym; Euflat-E†; Fermento duodenal; Hevertozym†; Kreon; Lipazym; Meteophyt forte†; Mezym F; Nutrizym N†; Ozym; Pangrol; Pankreatan; Pankreon; Panpeptal N; Panpur; Panzynorm forte-N; Panzytrat; Tryptoferm†; Unexym mono; ***Gr.:*** Creon; Pancrease; Panzytrat; ***Hong Kong:*** Creon; ***Hung.:*** Kreon; Mezym Forte; Neo-Panpur; Pangrol; Panzytrat; ***India:*** Biopank†; Festal N; Panstal N; Panzynorm-N; ***Irl.:*** Creon; Nutrizym; Pancrease†; Pancrex†; ***Israel:*** Creon; Pancrease; ***Ital.:*** Creon; Enzipan; Krebsilasi†; Luitase†; Pancrease; Pancrex; ***Malaysia:*** Creon; ***Mex.:*** Creon; Kenyna; Opti-Free; Opti-Free Supra Clens; Pancrease; Selecto†; Trepetan; ***Neth.:*** Cotazym-S†; Creon; Pancrease; Pancrease HL; Panzytrat; ***Norw.:*** Creon; Pancrease; Pankreon†; ***NZ:*** Cotazym; Creon; Pancrease; Pancrex; Panzytrat; ***Philipp.:*** Creon; ***Pol.:*** Kreon; Lipancrea; Neo-Pancreatinum; Panzytrat; ***Port.:*** Kreon; ***Rus.:*** Enzystal (Энзистал); Festal (Фестал); Kreon (Креон); Mezym Forte (Мезим Форте); Mikrazym (Микразим); Normoenzym Forte (Нормоэнзим Форте); Panzynorm (Панзинорм); Panzytrat (Панцитрат)†; Penzital (Пензитал); ***S.Afr.:*** Creon; Pankrease; Polyzym; Viokase; ***Singapore:*** Creon; Norzyme; ***Spain:*** Kreon; Pancrease; Papine; ***Swed.:*** Creon; Pancrease; Pankreon†; ***Switz.:*** Creon; Panzytrat; Prolipase†; ***Thai.:*** Creon; ***Turk.:*** Festal N; Kreon; ***UK:*** Clen-Zym; Creon; Nutrizym; Pancrease HL; Pancrease†; Pancrex; ***USA:*** Creon; Dygase; Enzymatic Cleaner; Ku-Zyme HP; Lapase; Lipram; Opti-Zyme; Palcaps; PAN-2400; Pancrease; Pancrecarb; Panocaps; Ultrase; Viokase; Vision Care Enzymatic Cleaner; ***Venez.:*** Orozim; Pancrease†; Pankreon.

Multi-ingredient: ***Arg.:*** Arnol; Bibol Leloup; Bil 13 Enzimatico; Biletan Enzimatico; Biluen Enzimatico; Carbogasol Digestivo; Digenorflat; Digesplen; Dom-Polienzim; Facilgest†; Faradil Enzimatico; Gastridin-E; Gastrimet Enzimatico†; Gastron Fuerte†; Hepadigenor†; Homocisteon Compuesto; Moperidona Enzimatica; Mosar Enzimatico; Novodig†; Pakinase; Pankreoflat; Pankreoflat Sedante†; Pankreon Compuesto†; Pankreon Total; Polienzim; Praxis; Pulsar Enzimatico†; Tridigestivo Soubeiran; ***Austral.:*** Digestaid; Enzyme; Lexat†; Prozyme†; ***Austria:*** Arca-Enzym; Combizym; Combizym Compositum; Enzyflat†; Gingivan; Helopanflat; Helopanzym; Intestinol; Ora-Gallin; Pankreoflat; Paspertase; Rennie Digestif; Wobenzym; ***Belg.:*** Digestomen; ***Braz.:*** Azime†; Combizym Composto†; Dasc; Digecap-Zimatico; Digeplus; Elozima†; Enziprid†; Essen; Filogaster†; Hepatoregius†; Nutrizim†; Pankreoflat; Peptopancreasi; Plasil Enzimatico; Primeral; Sintozima; ***Canad.:*** Digesta; ***Chile:*** Combizym Compositum; Digenil; Flapex E; Hepabil; Neopankreoflat; Nutrizima; Onoton†; ***Cz.:*** Combizym Compositum; Digestif Rennie; Wobenzym; ***Fin.:*** Combizym; Combizym Compositum; ***Ger.:*** Arbuz†; Chol-Arbuz NF; Combizym Compositum†; Combizym†; Enzym-Lefax; Enzym-Wied†; Meteozym; Pankreoflat; Pascopankreat; Paspertase†; Unexym MD S; Ventracid N; Wobenzym N; ***Hong Kong:*** Combizym; Digezym; Pankreoflat†; Topase†; ***Hung.:*** Combizym Compositum†; Combizym†; Digestif Rennie; Dipankrin; Pankreoflat; ***India:*** Biohep†; Digeplex-T; Dipep; Dispeptal†; Farizym; Hepa-Merz; Ipental†; Merckenzyme; Pankreoflat; Panolase†; Papytazyme; ***Indon.:*** Benozym; Berzymplex; Cotazym Forte; Elsazym; Enzymfort; Excelase-E; Librozym; Librozym Plus; Nutriflam; Pankreoflat; Pankreon Comp; Pankreon for Children; Primperan Compositum; Tripanzym; Vitazym; Xepazym; ***Israel:*** Encypalmed; Pankreoflat; ***Ital.:*** Combizym†; Digestopan†; Ede 6†; Essen Enzimatico†; Eudigestio†; Pancreoflat†; Pancresil†; Pepto-Pancreas†; ***Malaysia:*** Biotase; ***Mex.:*** Difarben; Dirfaben†; Dixiflen; Espaven Enzimatico; Ochozim; Onoton; Pankreoflat; Plasil Enzimatico; Selecto-D†; Wobenzym; Zimeton; Zimotris; ***Neth.:*** Combizym; ***Norw.:*** Combizym; ***NZ:*** Combizym†; ***Philipp.:*** Pankreoflat; Spasmo-Canulase; ***Pol.:*** Combizym; Hepa-Merz; ***Port.:*** Colerin-F; Combizym; Combizym Compositum†; Espasmon Canulase; Fermetone Composto; Helopanflat; Pankreoflat; ***Rus.:*** Ipental (Ипентал); Pankreoflat (Панкреофлат); Wobenzym (Вобэнзим); ***S.Afr.:*** Pankreoflat; Spasmo-Canulase; ***Singapore:*** Biotase; ***Spain:*** Digestomen Complex; Nulacin Fermentos; Pankreoflat; Wobenzimal†; ***Swed.:*** Combizym; Combizym Compositum; ***Switz.:*** Combizym; Combizym Compositum; Fermento duodenal†; Helopanflat†; Spasmo-Canulase; ***Thai.:*** Combizym; Combizym Compositum; Enzymet; Gaszym; Papytazyme†; Pepsitase; Polyenzyme-I; Polyenzyme-N; Proctase-P; Sanzyme-S†; ***Turk.:*** Flaton; Hazmolin; Intestinol; Multanzim; Pankreoflat; Pankrodigest; ***UK:*** Enzyme Digest; Enzyme Plus; ***USA:*** Digepepsin; Hi-Vegi-Lip; Pangestyme; ***Venez.:*** Combizym Forte; Nutizym Compositum; Pankreon Compositum; Pankreosil; Stamyl; Wobenzym N.

Pancreozymin *(BAN)*

CCK-PZ; Pancreocimina; Pankreotsymiini; Pankreozymin.

ATC — V04CK02.

ATC Vet — QV04CK02.

NOTE. The endogenous hormone is known as cholecystokinin (CCK).

Units

The potency of pancreozymin may be expressed as Crick-Harper-Raper units based on the pancreatic secretion in *cats* or as Ivy *dog* units based on the increase in gallbladder pressure. One Ivy dog unit is considered to be approximately equivalent to 1 Crick-Harper-Raper unit.

Profile

Pancreozymin is a polypeptide hormone prepared from the duodenal mucosa of *pigs*. When given by intravenous injection it