Preparations

Proprietary Preparations (details are given in Part 3)

Multi-ingredient: ***Fr.:*** Cosmodex Depigmenten†; ***Ital.:*** Anasterol; Lenirose†; Mavipiu†; ***Jpn:*** Q & P; Sin Q & P Gold; ***Singapore:*** Gin-Vita.

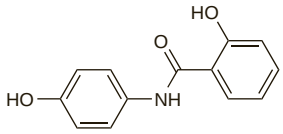
Osalmid *(rINN)*

L-1718; Osalmida; Osalmide; Osalmidum; Oxaphenamide. 4′-Hydroxysalicylanilide.

Осальмид

$C_{13}H_{11}NO_3$ = 229.2.

CAS — 526-18-1.



Profile

Osalmid has been used as a choleretic.

Otilonium Bromide *(BAN, rINN)*

Bromuro de otilonio; Octylonium Bromide; Otilonii Bromidum; Otilonium, Bromure d'; SP-63. Diethylmethyl{2-[4-(2-octyloxybenzamido)benzoyloxy]ethyl}ammonium bromide.

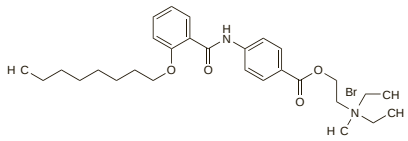
Отилония Бромид

$C_{29}H_{43}BrN_2O_4$ = 563.6.

CAS — 26095-59-0.

ATC — A03AB06.

ATC Vet — QA03AB06.



Profile

Otilonium bromide is used in the symptomatic treatment of gastrointestinal disorders associated with smooth muscle spasms in oral doses up to 120 mg daily. It has also been given rectally and by nebuliser.

◊ References.

1. Battaglia G, *et al*. Otilonium bromide in irritable bowel syndrome: a double-blind, placebo-controlled, 15-week study. *Aliment Pharmacol Ther* 1998; **12:** 1003–10.

Preparations

Proprietary Preparations (details are given in Part 3)

Arg.: Pasminox; Spasmoctyl; ***Belg.:*** Spasmomen; ***Braz.:*** Lonium; ***Cz.:*** Spasmomen; ***Gr.:*** Doralin; ***Hong Kong:*** Spasmomen; ***Hung.:*** Spasmomen; ***Indon.:*** Spasmomen; ***Ital.:*** Spasen; Spasmomen; ***Port.:*** Spasmomen; ***Spain:*** Spasmoctyl.

Multi-ingredient: ***Arg.:*** Pasminox Somatico; ***Ital.:*** Spasen Somatico; Spasmomen Somatico.

Oxaceprol *(rINN)*

Acetylhydroxyproline; C061; Oxacéprol; Oxaceprolum. (–)-1-Acetyl-4-hydroxy-L-proline.

Оксацепрол

$C_7H_{11}NO_4$ = 173.2.

CAS — 33996-33-7.

ATC — D11AX09; M01AX24.

ATC Vet — QD11AX09; QM01AX24.

Profile

Oxaceprol is reported to affect connective tissue metabolism and has been used in dermatology, to promote wound healing, and in rheumatic disorders. Adverse effects have included gastric pain, nausea, diarrhoea, dizziness, headache, and skin rashes.

◊ References.

1. Bauer HW, *et al*. Oxaceprol is as effective as diclofenac in the therapy of osteoarthritis of the knee and hip. *Clin Rheumatol* 1999; **18:** 4–9.
2. Herrmann G, *et al*. Oxaceprol is a well-tolerated therapy for osteoarthritis with efficacy equivalent to diclofenac. *Clin Rheumatol* 2000; **19:** 99–104.

Preparations

Proprietary Preparations (details are given in Part 3)

Arg.: Joint†; ***Fr.:*** Jonctum; ***Ger.:*** AHP 200; ***Spain:*** Tejuntivo.

Multi-ingredient: ***Spain:*** Robervital.

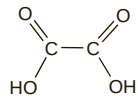
Oxalic Acid

Kwas szczawiowy; Oxálico, ácido.

$HO_2C,CO_2H,2H_2O$ = 126.1.

CAS — 144-62-7 (anhydrous oxalic acid); 6153-56-6 (oxalic acid dihydrate).

ATC Vet — QP53AG03.



Adverse Effects

On ingestion, severe gastroenteritis is produced by the corrosive action of oxalic acid and its soluble salts on the gastrointestinal tract. Burning of the mouth, throat, and oesophagus with ulceration may also occur. Hypoxia may occur in the presence of laryngeal oedema, and shock and hypotension may arise in severe cases. Oxalates can chelate body calcium following systemic absorption, and may produce symptoms of hypocalcaemia such as tetany, convulsions, and, in some cases, ventricular fibrillation. Oxalate crystals may be deposited in the blood vessels, brain, heart, liver, and lungs; deposition in the renal tubules leads to acute renal failure. The mean fatal dose of oxalates has been reported to be about 15 to 30 g, although death has occurred with much lower doses. Death may occur within a few hours of ingestion.

◊ Fatalities have resulted from intravenous administration of sodium oxalate[1] or ingestion of oxalic acid.[2]

Crystals of calcium oxalate present in the sap of daffodils[3] or *Agave tequilana* plants[4] have been reported to contribute to the rash experienced by workers coming into contact with these plants.

1. Dvořáčková I. Tödliche Vergiftung nach intravenöser Verabreichung von Natriumoxalat. *Arch Toxikol* 1966; **22:** 63–7.
2. Farré M, *et al*. Fatal oxalic acid poisoning from sorrel soup. *Lancet* 1989; **ii**: 1524.
3. Julian CG, Bowers PW. The nature and distribution of daffodil pickers' rash. *Contact Dermatitis* 1997; **37:** 259–62.
4. Salinas ML, *et al*. Irritant contact dermatitis caused by needle-like calcium oxalate crystals, raphides, in Agave tequilana among workers in tequila distilleries and agave plantations. *Contact Dermatitis* 2001; **44:** 94–6.

Treatment of Adverse Effects

After ingestion of oxalic acid, a dilute solution of any soluble calcium salt should be given to precipitate the oxalate; alternatively milk may be given. Oral activated charcoal has also been suggested if ingestion has occurred within 1 hour. Gastric lavage is contra-indicated by some centres given the corrosive nature of oxalic acid. Calcium gluconate 10% should be given intravenously to prevent tetany. Acute renal failure should be anticipated in surviving patients and calls for careful fluid management. Haemodialysis or peritoneal dialysis have also been suggested for the removal of oxalate in primary oxalosis in an attempt to prevent acute renal failure and correct hypocalcaemia.

Uses

Oxalic acid has varied industrial uses and has been used in escharotic preparations. Oxalic acid salts have been given orally and the urinary excretion of oxalate used as a screening test for lipid malabsorption.

Diagnostic use. References.

1. Rampton DS, *et al*. Screening for steatorrhoea with an oxalate loading test. *BMJ* 1984; **288:** 1419. Correction. *ibid.*; 1728.
2. Sangaletti O, *et al*. Urinary oxalate recovery after oral oxalic acid load: an alternative method to the quantitative determination of stool fat for the diagnosis of lipid malabsorption. *J Int Med Res* 1989; **17:** 526–31.

Preparations

Proprietary Preparations (details are given in Part 3)

Multi-ingredient: ***Cz.:*** Solcogyn†; ***Ger.:*** Solco-Derman; ***Hong Kong:*** Solcoderm; ***Malaysia:*** Solcoderm†; ***Pol.:*** Solcogyn; ***Rus.:*** Solcoderm (Солкодерм); Solcovagin (Солковагин); ***Switz.:*** Solcoderm; Solcogyn.

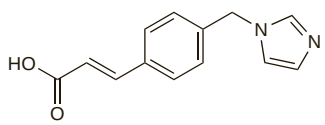
Ozagrel *(rINN)*

OKY-046 (ozagrel hydrochloride); Ozagrelum. (*E*)-*p*-(Imidazol-1-ylmethyl)cinnamic acid.

Озагрел

$C_{13}H_{12}N_2O_2$ = 228.2.

CAS — 82571-53-7.



Profile

Ozagrel is a thromboxane synthetase inhibitor that has been given orally as the hydrochloride for the treatment of asthma in doses of 200 mg twice daily. It has also been given as the sodium salt by intravenous infusion for the treatment of cerebrovascular disorders in a dose of 80 mg.

Preparations

Proprietary Preparations (details are given in Part 3)

Jpn: Cataclot; Domenan; Xanbon.

Palifermin *(USAN, rINN)*

AMJ-9701; Palifermina; Palifermine; Paliferminum; rHu-KGF. 24-163 Fibroblast growth factor 7 (human).

Палифермин

CAS — 162394-19-6; 178254-26-7.

ATC — V03AF08.

ATC Vet — QV03AF08.

Adverse Effects

Adverse reactions reported with palifermin therapy have included rash, erythema, oedema, pruritus, perioral dysaesthesia, tongue discoloration and thickening, and altered taste. Fever, and gastrointestinal and respiratory disturbances have also been reported. The safety and efficacy of palifermin in patients given treatment for non-haematological neoplasms has not been established; stimulation and growth of tumour cell lines have been found in *animal* and *in-vitro* models of non-haematopoietic human tumours.

Pharmacokinetics

The pharmacokinetics of palifermin were approximately dose-linear after a single intravenous dose in healthy subjects given larger than usual doses. The terminal elimination half-life is about 4.5 hours.

◊ References.

1. Zia-Amirhosseini P, *et al*. Pharmacokinetics, pharmacodynamics, and safety assessment of palifermin (rHuKGF) in healthy volunteers. *Clin Pharmacol Ther* 2006; **79:** 558–69.
2. Gillespie B, *et al*. Effect of renal function on the pharmacokinetics of palifermin. *J Clin Pharmacol* 2006; **46:** 1460–8.

Uses and Administration

Palifermin is a human recombinant keratinocyte growth factor (KGF) used to reduce the incidence and duration of severe oral mucositis (p.640) in patients with haematological neoplasms who receive myelotoxic chemotherapy, with or without radiotherapy, followed by haematopoietic stem cell transplantation. The recommended course of palifermin is 6 doses of 60 micrograms/kg, by intravenous bolus injection. A dose is given on each of 3 consecutive days before, and 3 consecutive days after, myelotoxic therapy. Palifermin should not be given during, or for 24 hours before or after, myelotoxic therapy. Thus, the third pre-chemotherapy dose of palifermin should be given 24 to 48 hours before myelotoxic therapy, and the first post-chemotherapy dose of palifermin should be given after, but on the same day as, the haematopoietic stem cell infusion, and at least 4 days after the third pre-myelotoxic dose.

Mucositis. Palifermin is a human recombinant keratinocyte growth factor (KGF) that binds to KGF receptors and repairs damaged epithelium by stimulating the proliferation, differentiation, and migration of epithelial cells.[1,2] Controlled studies have shown it to be effective in reducing the severity and duration of oral mucositis (p.640) in patients receiving myelotoxic therapy for haematological neoplasms and requiring haematopoietic stem cell support.[3,4] It has also shown benefit compared with placebo in reducing the incidence of oral mucositis and diarrhoea in patients receiving fluorouracil and leucovorin for metastatic colorectal cancer.[5]

1. Siddiqui MAA, Wellington K. Palifermin: in myelotoxic therapy-induced oral mucositis. *Drugs* 2005; **65:** 2139–46.
2. McDonnell AM, Lenz KL. Palifermin: role in the prevention of chemotherapy- and radiation-induced mucositis. *Ann Pharmacother* 2007; **41:** 86–94.
3. Spielberger R, *et al*. Palifermin for oral mucositis after intensive therapy for hematologic cancers. *N Engl J Med* 2004; **351:** 2590–8.
4. Stiff PJ, *et al*. Palifermin reduces patient-reported mouth and throat soreness and improves patient functioning in the hematopoietic stem-cell transplantation setting. *J Clin Oncol* 2006; **24:** 5186–93.
5. Rosen LS, *et al*. Palifermin reduces the incidence of oral mucositis in patients with metastatic colorectal cancer treated with fluorouracil-based chemotherapy. *J Clin Oncol* 2006; **24:** 5194–5200.

Preparations

Proprietary Preparations (details are given in Part 3)

Austral.: Kepivance; ***Cz.:*** Kepivance; ***Fin.:*** Kepivance; ***Fr.:*** Kepivance; ***Gr.:*** Kepivance; ***Hung.:*** Kepivance; ***Irl.:*** Kepivance; ***Neth.:*** Kepivance; ***Pol.:*** Kepivance; ***Port.:*** Kepivance; ***Swed.:*** Kepivance; ***UK:*** Kepivance; ***USA:*** Kepivance.

Palmarosa

Profile

Palmarosa (*Cymbopogon martini*, Poaceae) is a source of palmarosa oil (Indian geranium oil, Turkish geranium oil). Palmarosa oil is used in perfumery and in aromatherapy.

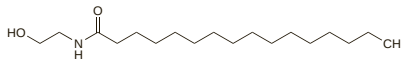
Palmidrol *(rINN)*

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).