Position Statement: Pancreatic enzyme replacement therapy (PERT) shortage – advice for clinicians on the management of adults with pancreatic exocrine insufficiency

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Position statement and advice for prescribers from the [1]Nutrition Interest Group of the Pancreatic Society of Great Britain and Ireland (NIGPS), [2] Cystic Fibrosis Specialist Group and [3] Gastroenterology Specialist Group, British Dietetic Association.

Endorsed by the British Society of Gastroenterology (Pancreas section); Pancreatic Society of Great Britain and Ireland, Pancreatic Cancer UK, GUTS UK, Cystic Fibrosis Trust, CF Medical Association, Pancreatic Cancer Action, Neuroendocrine Cancer UK and the British Dietetic Association.

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Please ensure you are reading the most up to date version, which is available on the Pancreatic Society of Great Britain and Ireland website:

https://www.psgbi.org/position-statement-pert-shortage/

This document has been extensively revised to include the imported medications that are available to fill the gap in supply of UK licenced products. It is expected that with this, no patient needing PERT should go without it.

Introduction

The ongoing supply issues surrounding pancreatic enzyme replacement therapy (**PERT)** preparations under the product brands: **Creon®**, **Nutrizym®** and **Pancrex®**) is predicted to continue until the end of 2026. However, the UK is now well supplied by imports of other preparations of PERT which are suitable for use as an alternative. This position paper is designed to meet the needs of the clinicians' managing patients with pancreatic exocrine insufficiency (PEI) and provides advice for prescribers and dietitians. A separate document is available providing advice for patients.

Pancreatic enzyme replacement therapy is prescribed to support adequate digestion in patients with PEI, most commonly due to pancreatic cancer, pancreatitis, pancreatic surgery, cystic fibrosis (CF) and neuroendocrine cancers – also known as neuroendocrine tumours (NET). There are many other clinical situations where patients may have primary or secondary PEI, such as following gastrectomy or gastric bypass surgery (1). Patients who take somatostatin analogues [Lanreotide (Somatuline®) / Octreotide (Sandostatin®)] for the treatment of neuroendocrine tumours (NETs) are also at risk of PEI. Regardless of aetiology, the impact of maldigestion varies from person to person in both the type of symptoms and their severity.

Symptoms of untreated PEI may include bloating, excess wind, diarrhoea, crampy abdominal pain, faecal urgency, steatorrhoea (pale floating stools), hard to manage blood glucose levels, vitamin and mineral deficiencies, weight loss and malnutrition (1). These symptoms are usually managed with PERT and will recur if patients are unable to take adequate doses.

There are many clinical impacts of inadequate PERT, which will affect all patients, and the advice in this document is targeted at all patient groups.

The advice in this paper may be updated as we receive further guidance. The most up to date version will be available at: https://www.psgbi.org/position-statement-pert-shortage/

Please note the advice in this document is designed for adults with PEI, specialist advice should be sought for children with PEI. Patients with cystic fibrosis will be under the care of a specialist centre, and they should contact their specialist team if they have any concerns.

Customer Services

The two main suppliers of PERT in the UK have set up customer support lines to help identify areas with recent deliveries. However, it is possible these deliveries may have already been allocated to specific patients.

- Viatris (Creon®) 0800 8086410 (for patients and pharmacists)
- Zentiva (Nutrizym®): 08448 793188 (for pharmacists) and 08000 902408 (for patients)

Advice for Prescribers

The current supplies of PERT available through the normal prescribing routes are not sufficient to meet the needs of the UK population. At least 1 in 10 prescriptions will not be filled via this route**. Patients must not run out of these medications.** The advice in previous versions of this document has been revised as there is no longer a reason for patients to run out of PERT. **Hospitals no longer receive priority orders, so may not be able to issue rescue prescriptions.**

Each ICB has developed a plan for the medicine shortage in line with the NatPSA/2024/013/DHSC, and in most cases that includes the use of imported medication. These imports have been added to local Formulary's and to electronic prescribing databases, and in many places specific prescribing and dispensing advice has been issued.

If a patient has less than 2 weeks supply of PERT left, most ICBs are now recommending an imported medication is prescribed.

It is acknowledged that these imports are more expensive, but reimbursement is now in place for pharmacies. It is important to remember that this is an essential medication, and there will be detrimental health effects, increased need to access healthcare providers and considerable anxiety associated with undertreatment (2).

Where possible ICBs have imported medications that match the doses of existing medications to make it easier for prescribers and patients to use both interchangeably. There is no evidence to suggest that there is any difference between European and American units of enzymes in these preparations (3)

PERT product prioritisation:

- Creon Micro® is prioritised for infants and those with dysphagia who are also unable to open the Creon 25,000® capsules.
- Creon 10,000® should be prioritised for children and those unable to swallow larger capsules
- Nutrizym 22® has limited availability and should be prioritised for those unable to tolerate Creon preparations
- Pancrex V® powder should only be prescribed for patients receiving enteral feeding

Patients cannot "go without" this medication. This can have significant adverse health effects.

Logistical recommendations

- Liaise with your ICB (medicines management teams) regarding regional plans for imported medicines and accessing emergency supplies for patients who have run out.
- Allow an override of any electronic systems that block prescription requests if they are placed less than 4 weeks since the previous request: Patients should be advised to place their next prescription request as soon as the previous one has been dispensed to allow time for a supply to be sourced.
- If you have an "in house" pharmacy – identify if they are able to place orders that sit on a back-order list at the wholesalers, if not, leave prescriptions on the NHS Spine in order that patients can take these to a pharmacy that can.
- Please provide PERT prescriptions on singular prescriptions to allow patients to take prescriptions to a different pharmacy to those who dispense their other medicines.
- In line with the Medicines Supply Notification from the Department of Health and Social Care (issued 16/2/24 MSN/2024/022). Please ensure that only one-month supply is issued at a time. (4).

Clinical management suggestions to optimise efficiency of PERT:

- Taking PERT throughout the meal rather than all at the start/ middle/ end improves efficacy.
- For people with CF, please do not change medications, but seek advice from specialist teams.
- Consider prescribing a **proton pump inhibitor** or **H2 receptor antagonist** to reduce acid degradation of the PERT and optimise efficacy in patients where there are not any contra-indications (1).
- Consider prescribing a **multivitamin and mineral** and a **calcium and vitamin D supplement** if patients are not already taking one

CAUTIONS – impact of inadequate PERT on other medication / medical conditions

- **DIABETES**: Be aware that patients on insulin or oral hypoglycaemic agents that can cause hypoglycaemia may experience worsening control and be more susceptible to hypoglycaemia.
    - Patients with diabetes MUST NOT go without PERT – they are at risk of life-threatening hypoglycaemia.
    - Please ensure patients with diabetes have adequate testing equipment to allow for increased monitoring.
    - Patients on insulin should (subject to local guidelines) have continuous glucose monitoring devices and these should have the low glucose alarm set.
    - Patients should be encouraged to monitor glucose levels more frequently, especially when undertaking activities such as driving or exercise.
    - Patients who have had a total pancreatectomy are especially vulnerable to hypoglycaemia as they have an absence of glucagon as well as endogenous insulin.
- Please be aware that malabsorptive diarrhoea is osmotic and results in rapid transit time. This may impact the **absorption of other medication** (including medication prescribed for seizure control, anti-hypertensives, arrhythmia drugs, antibiotics and the oral contraceptive pill etc.,)
    - Secondary forms of contraception should be recommended.
    - Please increase monitoring for people with dose sensitive medication.
    - Use loperamide to reduce transit speed where necessary (Not for patients with CF – refer to specialist centre).
- **ANTI-COAGULATION:** Please be aware that Vitamin K is a fat-soluble vitamin and uptake maybe impaired with inadequate PERT – additional monitoring may be needed for patients on anti-coagulation where dietary Vitamin K should be regulated.
- **FALLS:** Uncontrolled PEI results in faecal urgency which is a risk factor for falls in vulnerable patients. Consider the use of loperamide to control faecal urgency where necessary.

CAUTIONS – differential diagnosis

- Distal intestinal obstruction syndrome (DIOS) is a unique feature of CF and is characterised by the accumulation of viscid mucofaecal material in the terminal ileum and caecum. Being a common complication in people with CF, it needs to be considered if someone with CF presents with symptoms following a change in their PERT prescription.
- Be aware that patients with small bowel NETs may be at risk of Carcinoid syndrome, mesenteric fibrosis, short bowel syndrome etc, please refer to their specialist teams if you have concerns.
- Consider that patients with PEI, may also have bile acid malabsorption, small intestinal bacterial overgrowth, coeliac disease etc., please investigate and treat in line with current guidelines (2).

IMPORTANT

For patients with CF please contact the patients' CF Specialist team. For all other patients please contact your local tertiary hepato-pancreatico-biliary (HPB) / pancreatic / neuroendocrine unit. Depending on the local service available, this may be either the specialist HPB / pancreatic / NET dietitian or pancreatologist. The Specialist Pharmacy Service Medicines Supply Tool can be accessed by Prescribers for more information on supply at: https://www.sps.nhs.uk

Advice for Dietitians

In addition to the above advice, please consider the following to optimise the use of PERT:

- Remind patients to spread the dose of their PERT out throughout their meals to optimise absorption – taking some PERT at the beginning, some in the middle and some towards the end of their meal.
- Remind patients to store their enzymes properly – all products should be stored below 25 degrees, and some require refrigeration. Excess heat causes irreversible denaturation.
- Refer patients not responding to treatment back to their managing physician to ensure other causes of diarrhoea have been excluded.
- When PERT doses have been escalated in response to ongoing symptoms, please ensure symptoms are re-evaluated. If a clinical benefit is not observed, please reduce the dose back down. If reducing the dose worsens symptoms, this is considered a clinical benefit of the higher dose, and doses should be returned to the higher doses which reduced symptoms.
- Consider using peptide based oral nutritional supplements (ONS). i.e., **VITAL 1.5 kcal®** / **Survimed OPD 1.5kcal®/ Peptisip Energy HP®** in place of polymeric supplements to reduce the need for PERT with polymeric ONS. **Peptamen® Vanilla** contains less energy (1kcal/ml), but these could be used if supplies of **VITAL 1.5 kcal®** / **Survimed OPD 1.5kcal®/ Peptisip Energy HP®** are limited.
- Consider fat free ONS sipped slowly without PERT if the patient is weight stable and does not have diabetes. If the patient experiences significant abdominal symptoms or weight loss despite this, please swap to peptide based ONS. PERT is still be required for polysaccharide and protein digestion. Fat free ONS are not nutritionally complete and should not be used a sole source of nutrition.
- Use **ProSource Jelly®** / **ProSource Plus®** / **ProSource 20®** for additional protein (as these are peptide based).
- Medium chain triglyceride (MCT) lipid products (**Liquigen®** / **MCT oil®**) could be used alongside fat free ONS in patients who need higher energy ONS. Please note that **Elemental 028®** contains 35% MCT and still requires PERT for lipid absorption. **Emsogen®** can also be considered, as this should not require PERT, but is low in energy and protein, this can be concentrated if tolerated.
- Ensure patients with diabetes on **insulin** or **Gliclazide** are regularly monitoring their blood glucose levels and aware of how to treat a hypo.
- Please ensure patients with signs of malabsorption and taking anti-coagulation are highlighted to their managing physician as Vitamin K absorption may be impaired.
- Seek advice from specialist centres for specific advice for patients with CF.
    - CF Dietitians will review and optimise PERT dosing and adherence.
    - CF Dietitians will optimise vitamins and minerals and adjust as appropriate.
- Patients with intractable malabsorption may need peptide enteral, or in severe cases parenteral nutrition.

Nutritional composition of additional products

Liquigen® 30mls = 136kcal, 0g protein, 97.4% MCT. ACBS approved. 250ml bottle, once open store in a refrigerator and use within 14 days. Suitable for vegans and vegetarians.

Nutricia MCT oil® 100mls = 855kcal, 0g protein, 99.9% MCT. ACBS approved. 500ml bottle, once open, reseal and use within 1 month. Suitable for vegans and vegetarians.

Vital 1.5kcal® 300kcal, 13.5g protein (as peptide), 64% MCT. ACBS approved. 200ml bottle, suitable for vegetarians (not vegan), once open store in a refrigerator and discard after 24 hours

Peptisip Energy HP® 300kcal, 15g protein (as peptide), 60% MCT, ACBS approved, 200ml bottle, suitable for vegetarians (not vegan), once open store in a refrigerator and discard after 24 hours.

Survimed® **OPD 1.5kcal** drink – 300kcal, 15g protein (as peptide), 50% MCT, ACBS approved, 200ml bottle, once open store in a refrigerator and discard after 24 hours.

Emsogen® 438 kcal, 12.5g protein per 100g,(as amino acid), 83% MCT, 88kcal per 100mls, 2.5g protein, ACBS approved. Note this is a low energy, low protein supplement drink. Standard concentration is 20% w/v (1 x 100g sachet in 500mls water). This can be concentrated further if tolerated, but patients may require additional fluids afterwards. Milkshake / coffee syrups can be added to flavour.

ProSource Jelly® 90kcal, 20g protein (as peptide), 0g fat, <1g carbohydrates, ACBS approved. 118g serving, serve chilled.

ProSource Plus® 100kcal, 15g protein (as peptide), 0g fat, 11g carbohydrates. ACBS approved. 30ml serving, flavoured products can be taken as a shot, unflavoured can be added to drinks or food.

Peptamen Vanilla® 200kcal, 8g protein (as peptide), 68% MCT, ACBS approved. 200ml bottle, best served chilled, once open refrigerate and consume within 24 hours.

References / sources of further information

1) Phillips ME, Hopper AD, Leeds JS, *et al* Consensus for the management of pancreatic exocrine insufficiency: UK practical guidelines *BMJ Open Gastroenterology* 2021 ;**8:**e000643. doi: 10.1136/bmjgast-2021-000643
2) https://gutscharity.org.uk/2024/11/sharing-the-results-from-our-pert-shortages-survey/
3) https://lp.thieme.de/emag/CP/11525-Drug-Report-Pankreatin-2024/#6
4) https://cks.nice.org.uk/topics/diarrhoea-adults-assessment/ accessed 16/3/24

Appendix 1: Content of imported pancreatin products

There are multiple options for imports. These are a selection of products available.

CREON® / KREON®

Creon (Kreon in Germany) can be imported in the same doses as licenced in the UK, we recommend this is done to reduce confusion for patients. (10,000 and 25,000)

PANGROL®

Enteric coated capsules with mini tabs

Preparation	Pack size	Presentation	Amylase	Protease	Lipase
Pangrol 10,000	200	Capsule	9000	500	10,000
Pangrol 25,000	200	Capsule	22,500	1250	25,000

Viokace®

Tablet presentation. Please note these contain Lactose.

Preparation	Pack size	Description	Amylase	Protease	Lipase
Viokace® Tablets Made by Nestle (Imported by Target)	100	Tablets – tan, round, biconvex VIO9111 on one side and 9111 on the other	39,150	39,150	10,440
	100	Tan, oval, biconvex with V16 on one side and 9116 on the other	78,300	78,300	20,880