

Creon (Pancrelipase)

Newborn use only

2025

Alert	Enzyme activity of Pancreatic Enzyme Replacement Therapy (PERT) is negligible in the gut after 3 hours of administration.
Indication	Pancreatic exocrine insufficiency, e.g. cystic fibrosis (CF).
Action	Pancreatic enzyme replacement. Granules (mini microspheres) are enteric coated and contain lipase, amylase and protease. Enteric coating of granules prevents them from disintegrating in acidic pH in stomach. When the granules reach the small intestine, the coating rapidly disintegrates (at pH > 5.5) to release enzymes. The granules are similar in size to food particles (0.7-1 mm in diameter), arrive in the duodenum simultaneously with the food or fluid and mix homogeneously with the chyme while being protected from inactivation by gastric acid (pH 1) for up to 2 hours. ¹
Drug Type	Porcine pancreatic extract containing lipase, amylase and protease.
Trade Name	Australia - Creon Micro (5,000). In Australia, Creon 10,000 is not advised for neonates. New Zealand – Creon 10,000
Presentation	Creon Micro (Australia) 20g bottle – Enteric coated granules . Each scoop (supplied) contains 5,000 IU lipase, 3,600 IU of amylase and 200 IU of protease. (1, 2) Granules size 0.7-1.0mm. ³ Creon 10,000 (New Zealand) – Capsules containing enteric coated granules. Each capsule contains 10,000 IU lipase, 8,000 IU of amylase and 600 IU of protease.(1, 2) Granules size 0.7-1.6mm. ³
Dose	<p><u>ANMF consensus (Extrapolated from 2017 ANZ guidelines and 2024 ESPGHAN guidelines)</u>^{2,4,5}</p> <p><u>Dose Calculated based on lipase units</u></p> <p><u>Infant on breastfeeds or bottle feeds</u> Initiate at 2,500-5,000 IU lipase (1/2 to full scoop of Creon Micro) per breastfeed or bottle feed. Adjust up according to weight gain and bowel symptoms. Maximum of 10,000 IU lipase/kg/day*</p> <p><u>Infant on intermittent tube feeds</u> Initiate at 500-2,000 IU lipase/g of fat/meal at the commencement of each feed through feeding tube. Example: 100 mL of breastmilk contains 3.5g fat. This equates to 1750-7000 units lipase/100 mL of breastmilk. Adjust according to weight gain and bowel symptoms. Maximum of 10,000 IU lipase/kg/day*</p> <p><u>Infant on continuous tube feeds</u> Calculate the lipase dose required for 2-4 hours' worth of feed depending on unit's policy on hang time (e.g. 500-2,000 IU lipase/g of fat) Adjust up according to weight gain and bowel symptoms Maximum of 10,000 IU lipase/kg/day*</p> <p>NOTE:</p> <ol style="list-style-type: none"> 1. PERT is to be given prior to feed wherever possible.⁶ 2. Creon is to be given immediately prior and no later than 30 minutes from the beginning of the oral/enteral feed to ensure appropriate enzyme activity.⁷ 3. If administered through feeding tube - Choose the biggest size feeding tube appropriate for the infant (smaller tubes can become blocked easily). 4. Granules may need to be crushed to administer via feeding tube. Enzymes may not be as efficient when crushed. Adjust up according to weight gain and bowel symptoms. Clinicians may consider proton pump inhibitors when crushed granules are administered to improve the efficacy of enzymes as crushing it loses the pH sensitive coating. <p>*In some situations, upper limit may exceed as per the advice from the CF team.</p>
Dose adjustment	Therapeutic hypothermia – Not applicable. ECMO – Not applicable Hepatic impairment – Not applicable.

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	Renal impairment – Not applicable.
Maximum Dose	10,000 IU lipase/kg/day* *In some situations, upper limit may exceed at times - this should be done in consultation with gastroenterologist and CF dietitian.
Route	ORAL Intragastric
Preparation	REFER to Administration and Appendix
Administration	<u>Refer to Appendix for detailed administration</u> <u>If PERT can be administered ORALLY</u> The measuring scoop provided with the bottle contains 100 mg of granules (5000 IU of lipase). Collect the prescribed dose of granules using the supplied scoop. Mix the granules with apple or pear puree (not juice) if infant can swallow and can be given by spoon. Where necessary, clear gums of residual enzymes to prevent irritation. Consider zinc-based cream to the buttocks and frequent diaper changes to prevent skin excoriation. <u>If PERT to be given via feeding tube</u> Use the biggest feeding tube possible so tube doesn't get blocked with granules. Measure the granules required using the supplied scoop (Full scoop = 5,000 IU lipase). Granules can be crushed immediately prior to administration and mixed with feed. ⁴ Administer the crushed granules through feeding tube immediately prior to, and/or during feeds. If on continuous feeds – Calculate the dose for 2–4-hour volume of feed as per unit's policy on hang time.
Monitoring	Observe for acute symptoms such as abdominal distension and steatorrhea. Weight, height and head circumference at regular intervals. ⁴
Contraindications	Patients who are known to be hypersensitive to porcine protein or any of the ingredients.
Precautions	Fibrosing colonopathy has been reported in CF patients treated with high doses. The mechanism of injury is unknown. Doses more than 10,000 IU lipase/kg/day should be used with caution and in consultation with gastroenterologist and CF dietitian. ¹
Drug Interactions	Antacids should not be taken concomitantly with PERT as the alkaline pH in the stomach may break down the enteric coating. It is recommended that at least one hour elapse between the intake of antacids and any PERT.
Adverse Reactions	Abdominal pain and discomfort Diarrhoea Vomiting Fibrosing colonopathy with doses >10,000 IU lipase/kg/day.
Overdose	AUSTRALIA Contact the Poisons Information Centre on 13 11 26 for information on the management of overdose. NEW ZEALAND Contact the National Poisons Centre on 0800 764 766 for information on the management of overdose.
Compatibility	Not applicable.
Incompatibility	Not applicable
Stability	Creon Micro – Use within 3 months of opening bottle Creon 10,000 – Use within 6 months of opening bottle
Storage	Store below 25°C. In warmer climates it may be necessary to store the product in the refrigerator. Keep the container tightly closed in order to protect from moisture.
Excipients	Creon Micro - Macrogol 4000, hypromellose phthalate, dimeticone 1000, triethyl citrate, cetyl alcohol. ¹ Creon 10,000: macrogol 4000, hypromellose phthalate, dimeticone 1000, cetyl alcohol, triethyl citrate, gelatin, iron oxide red, iron oxide black, iron oxide yellow and sodium lauryl sulfate.
Special Comments	
Evidence	Background Pancreatic insufficiency (PI) occurs in more than 85 % of the CF population. ⁴ PI refers to inability of the pancreas to secrete sufficient enzymes such as lipases, proteases and amylases to the duodenum. Exocrine PI starts in utero in CF. An impaired pancreatic bicarbonate secretion (HCO ₃ ⁻) results in a

prolonged acidic environment in the proximal duodenum after gastric emptying. PI can be diagnosed by low levels of measured faecal elastase-1 ($\leq 100 \mu\text{g/g}$ stool or borderline $100\text{--}200 \mu\text{g/g}$ stool).⁴ Pancreatic enzyme replacement therapy (PERT) is a therapy to correct nutrient maldigestion and malabsorption in PI. PERT contains lipase, protease and amylase. Currently all PERT products are porcine derived. PERT is available as enteric coated granules, enteric coated capsules containing granules or enteric coated tablets. Although amylase and protease secretion from the pancreas are also affected in PI, lipase is contained in large amounts in PERT because lipase is more readily denatured in duodenum compared to amylase or proteases.

Efficacy of PERT

Most studies for PERT efficacy utilize coefficient of fat absorption (CFA) to measure improvement in steatorrhea, and coefficient of nitrogen absorption (CNA) to quantify changes in azotorrhea. A meta-analysis on PERT's efficacy in adult patients with chronic pancreatitis showed that PERT significantly improved CFA and CNA, and among randomized controlled trials PERT improved GI symptoms and decreased faecal weight, faecal fat, and nitrogen excretion.⁸ A Cochrane review noted no high-quality trials comparing PERT to placebo in CF.⁹

Efficacy comparisons with different dosing schedules of PERT

There are no randomised controlled trials determining whether one dosing schedule for PERT is better than the other in improving fat absorption, nutritional status and quality of life.¹⁰ PERT dose can be determined in lipase units by patient weight or by the fat content of the meal. Practice in Australia and New Zealand is to recommend PERT based on grams of fat consumed.²

Efficacy in paediatric population

The Baby Observational and Nutrition Study (BONUS) was a prospective multi-centre study to assess growth, nutrition and other clinical outcomes in infants with CF during the first year of life at 28 US CF centres.¹¹ The study described the PERT practices among the centres and evaluated any associations between dosing and growth outcomes. Centres with a higher PERT dosing strategy did not yield any greater clinical benefit than dosing at the lower end of the recommended range.¹²

A 2018 retrospective study evaluated the relationship between the initial dose of PERT and weight gain over the first 2 years of life. Median weight at the commencement of PERT was about 4 Kg. An initial dose of $>1,500$ lipase units/kg/largest meal resulted in a higher likelihood of attaining weight-for-age z score (WAZ) at 2 years at or above the birth WAZ (adjusted odds ratio 1.87, 95% CI: 1.22–2.86) and at the top quartile for improvement over 2 years in WAZ (adjusted odds ratio 1.90, 95% CI 1.19–3.05).⁵

PERT dosing recommendations

Current European, American and Australasian guidelines recommend PERT dosage should be dependent on fat content in meals, with a daily maximum of 4,000 lipase units/g of fat or 10,000 lipase units/kg body weight/day.^{2,4,13,14}

2024 ESPEN-ESPGHAN-ECFS Guidelines

European Society of Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN), European Society for Clinical Nutrition and Metabolism (ESPEN), European Cystic Fibrosis Society (ECFS) working group on nutrition care of patients with CF recommend the following on PERT:⁴

1. Pancreatic enzymes shall be started in all patients who have evidence of exocrine PI.
2. The pH in small intestine determines the release of pancreatic enzymes from the enteric coated beads.
3. Evidence is lacking around routine use of proton pump inhibitors (PPI) to improve enzyme efficacy.
4. PERT dose may be done on an individual basis.

2017 Australian and New Zealand nutrition guidelines for cystic fibrosis recommendations:²

1. Assessment to determine PI should be coordinated by or managed in conjunction with a specialist CF gastroenterologist. In centres where a specialist CF gastroenterologist is not available, advice should be sought from a major CF centre for areas of uncertainty.
2. One of the common tests to determine PI in neonates is faecal elastase-1 test.
 - a. Faecal elastase is a pancreatic-specific protease that unlike chymotrypsin is not degraded by intestinal passage.
 - b. Faecal elastase-1 of $<100 \mu\text{g/g}$ is highly predictive of PI.
 - c. Faecal elastase-1 test requires only a single stool sample. Result is not affected by PERT and therefore can be useful in patients on PERT.

- d. Limitation is that false positive results can occur with non-pancreatic diarrhea due to dilution. It is also not suited to determine efficacy of PERT.
- 3. Current consensus guidelines recommend that people with CF take PERT before and/or during a meal.
- 4. **Practice in Australia and New Zealand is to recommend PERT based on grams of fat consumed.** This is due to:
 - a. Improvements in the CFA with this method compared to dosing per meal.
 - b. Dosing mimicking the body's physiological response to a meal.
- 5. Internationally, guidelines give recommendations for either units of lipase/meal or units of lipase/g of fat consumed. Dosing per meal has been used due to ease of adherence with this method compared to dosing per gram of fat intake.
- 6. Maximum daily dose: Dose not to exceed 10,000 IU lipase/kg/day, as higher doses were associated with fibrosing colonopathy.
- 7. PERT dosing recommendations for neonates:
 - a. **Neonates on Parenteral nutrition (PN):** Discuss initiation of PERT with the neonatal team if titrating from PN onto oral and/or enteral feeds. PERT is often commenced when enteral or oral feeds are at 50% of the target volume.
 - b. Initiate at 2,500-5,000 IU lipase per breastfeed or formula feed, or 2,000 IU lipase/g fat. Then, adjust the dose according to weight gain and bowel symptoms.
- 8. There is little evidence to support how PERT is best administered in neonates on enteral nutrition. Several techniques have been described including:
 - a. ORAL administration
 - b. PERT suspended in acidic fruit puree (e.g. apple puree) or juice (e.g. apple juice)
 - c. Administration of crushed granules via an enteral feeding tube
 - d. PERT dissolved in bicarbonate and administered via an enteral feeding tube
- 9. **Continuous feeds:** A few dosing options have been described including:
 - a. Calculating the dose in units of lipase/g of fat/DAY and then divide the total daily dose into multiple doses every 3 hours during a feed
 - b. PERT enzyme activity in the gut is negligible after 2-3 hours and it may be appropriate to administer a lipase dose which matches the amount of fat to be delivered over 2-3 hours of continuous feeding.

Steps of PERT activation mechanism:²

1. PERT is usually administered orally with fat containing food/fluid with the aim of arriving in the duodenum simultaneously with the food or fluid.
2. Enteric coated granules are mixed with food in the stomach.
3. Enteric coating protects the enzymes from gastric acid.
4. Intact enteric coated enzymes pass through pylorus into duodenum.
5. Alkaline environment in the duodenum dissolves the enteric coating and active enzymes are released.

Efficacy of PERT granules and duodenal pH

An alkaline environment (e.g. pH >5.5) is essential for disintegration of coating and release of enzymes. The enteric coating of the granules will not break down if the pH is below 5.5. At the same time, the amount of viable pancreatic lipase is reduced as pH decreases, ceasing altogether at a pH below 4. The pancreas normally secretes concentrated bicarbonate to ensure that its enzymes are provided with the right environment, but in PI this function is impaired. Gastric acid hypersecretion occurs with many GI disorders, and this can denature the pancreatic enzymes, causing malabsorption.⁷ In theory, acid suppression medication as an adjunct therapy to PERT may increase the pH of the duodenum, to aid acid neutralization and subsequently assisting PERT function therefore improving fat digestion and absorption. However, a 2021 Cochrane review showed limited evidence that agents that reduce gastric acidity are associated with improvement in gastro-intestinal symptoms and fat absorption, but insufficient evidence to indicate whether there is an improvement in nutritional status, lung function, quality of life, or survival.¹⁶

PERT administration through feeding tubes (crushed or uncrushed)

Administration of PERT granules through feeding tube can be problematic due to blockage and the loss of enzyme's effects. To maximize absorption and reduce the risk of tube blockage, it is important to consider the size of the feeding tube, its position in the gut, and the type of feeding regimen (whether continuous, intermittent, or bolus). Some loss of enzyme activity is likely with this method, and dosage should be adjusted to compensate.

Gastric tube feeds: When PERT granules are to be given into a gastric feeding tube – granules are ideally left whole so that the enteric coating can protect the enzyme activity from gastric acid. However intact granules can block the smaller feeding tube (<10Fr size). Ferrie et al and Grunert et al described PERT administration in these scenarios.^{3,7,15}

Gastric tube size ≥10 Fr: Giving these granules in water can clump in the feeding tube, causing a blockage, whereas the use of a thickened acidic fluid, such as mildly thickened or “nectar”- consistency fruit juice (of any type of fruit) has the advantages of maintaining the enteric coating and keeping the granules suspended and not clumped.⁷

Gastric tube size <10Fr: Use of thickened juice is not considered appropriate in extremely preterm infants with small bore feeding tubes. Granules can be crushed and added to the feed immediately prior to the administration of feed. With this method, the enzymes are activated in the feed resulting in a “pre-digested” formulation, which negates the need to keep the outer enteric coating on the enzyme beads intact when they reach the stomach and are exposed to gastric acid.¹⁵

Duodenal or jejunal tube feeds: **Option 1:** Granules can be crushed to make an activated enzyme solution and if appropriate, can be mixed with sodium bicarbonate. Sodium bicarbonate (10 mL of 8.4% sodium bicarbonate per each 10,000 IU of lipase) creates an alkaline environment and granules' coating is completely dissolved to release the enzymes. This solution (that is crushed enzymes with or without sodium bicarbonate) can be either given directly into feeding tube via syringe or mixed with enteral feed, so “pre-digested” feed is administered through the feeding tube. **Option 2:** Uncrushed granules can be mixed with the bicarbonate solution and allowed to stand until the enteric coating dissolves spontaneously; this takes about 20 minutes. However, large volumes of sodium bicarbonate solution are not considered appropriate for most neonates.

Proton pump inhibitors (PPIs) with PERT

In practice clinicians may use PPIs to optimize the function PERT. With sufficient gastric acid suppression, it may be possible to give crushed, alkaline-activated enzyme (either as a solution or mixed in enteral feeds) into a gastric tube. This may be a preferred method for small-bore feeding tubes (smaller than 10-Fr) that could be blocked by whole granules.⁷ However, a 2021 Cochrane review showed limited evidence that agents that reduce gastric acidity are associated with improvement in gastro-intestinal symptoms and fat absorption, and insufficient evidence to indicate whether there is an improvement in nutritional status, lung function, quality of life, or survival.¹⁶ One trial included in this review showed decreased faecal fat loss in CF children on high dose PERT (>10,000 IU lipase/kg/d) after 10-20 mg daily omeprazole for one month,¹⁷ but 2nd trial using ranitidine and/or omeprazole as adjuvant therapy to PERT in children and adults with CF showed no benefit on fat absorption.¹⁸

Pharmacokinetics

Enzyme activity in the gut is negligible after 2-3 hours of administration of PERT.²

Safety

Fibrosing colonopathy has been reported in CF patients treated with high doses. The mechanism of injury is unknown. A maximum dose of 10,000 IU lipase/kg/day was recommended following observations that doses above 6,000 IU lipase/kg/meal and a mean of 50,000 IU lipase/kg/day were associated with fibrosing colonopathy. While this maximum is still generally accepted, the median dose in the control group of the US case-control study investigating fibrosing colonopathy was 13,393 IU lipase/kg/day, giving rise to the idea that this maximum may be too conservative. Neonates may feed up to 12 times per day and therefore may exceed the maximum recommended dose of 10,000 IU lipase/kg/day at times. It can also be challenging to remain below the maximum suggested dose in infants with high fat diets or who are on oral or enteral nutrition support. While there is some suggestion that the maximum of 10,000 IU lipase/kg/day may be exceeded without harm in the short term, this should be done with caution and in consultation and regular review with an experienced gastroenterologist and dietitian. Longer term studies are required to determine whether exceeding the suggested upper limit of 10,000 IU lipase/kg/day for an extended period is safe.²

Practice points	
References	<ol style="list-style-type: none"> 1. Creon Micro. MIMS online. Accessed on 15 April 2025. 2. Saxby N, Painter C, Kench A, King S, Crowder T, van der Haak N. and the Australian and New Zealand Cystic Fibrosis Nutrition Guideline Authorship Group (2017). Nutrition Guidelines for Cystic Fibrosis in Australia and New Zealand, ed. Scott C. Bell, Thoracic Society of Australia and New Zealand, Sydney. 3. Grunert J. Protocol for PERT administration with enteral feeds. Women's and Children's Hospital, South Australia, September 2012. 4. Wilschanski M, Munck A, Carrion E, Cipolli M, Collins S, Colombo C, et al. ESPEN-ESPGHAN-ECFS guideline on nutrition care for cystic fibrosis. <i>Clinical Nutrition</i>. 2024;43(2):413-45. 5. Schechter MS, Michel S, Liu S, Seo BW, Kapoor M, Khurmi R, et al. Relationship of initial pancreatic enzyme replacement therapy dose with weight gain in infants with cystic fibrosis. <i>Journal of Pediatric Gastroenterology and Nutrition</i>. 2018;67(4):520-6. 6. Freswick PN, Reid EK, Mascarenhas MR. Pancreatic enzyme replacement therapy in cystic fibrosis. <i>Nutrients</i>. 2022;14(7):1341. 7. Ferrie S, Graham C, Hoyle M. Pancreatic enzyme supplementation for patients receiving enteral feeds. <i>Nutrition in Clinical Practice</i>. 2011;26(3):349-51. 8. de la Iglesia-García D, Huang W, Szatmary P, Baston-Rey I, Gonzalez-Lopez J, Prada-Ramallal G, et al. Efficacy of pancreatic enzyme replacement therapy in chronic pancreatitis: systematic review and meta-analysis. <i>Gut</i>. 2017;66(8):1354-5. 9. Somaraju URR, Solis-Moya A. Pancreatic enzyme replacement therapy for people with cystic fibrosis. <i>Cochrane Database of systematic reviews</i>. 2020(8). 10. Ng C, Major G, Smyth AR. Timing of pancreatic enzyme replacement therapy (PERT) in cystic fibrosis. <i>Cochrane Database of Systematic Reviews</i>. 2021(8). 11. Leung DH, Heltshe SL, Borowitz D, Gelfond D, Kloster M, Heubi JE, et al. Effects of diagnosis by newborn screening for cystic fibrosis on weight and length in the first year of life. <i>Jama, Pediatr</i>. 2017;171(6):546-54. 12. Gelfond D, Heltshe SL, Skalland M, Heubi JE, Kloster M, Leung DH, et al. Pancreatic enzyme replacement therapy use in infants with cystic fibrosis diagnosed by newborn screening. <i>Journal of pediatric gastroenterology and nutrition</i>. 2018;66(4):657-63. 13. Stallings VA, Stark LJ, Robinson KA, Feranchak AP, Quinton H, on Growth CPG, et al. Evidence-based practice recommendations for nutrition-related management of children and adults with cystic fibrosis and pancreatic insufficiency: results of a systematic review. <i>Journal of the American Dietetic Association</i>. 2008;108(5):832-9. 14. Turck D, Braegger CP, Colombo C, Declercq D, Morton A, Pancheva R, et al. ESPEN-ESPGHAN-ECFS guidelines on nutrition care for infants, children, and adults with cystic fibrosis. <i>Clinical nutrition</i>. 2016;35(3):557-77. 15. Grunert J, Tai A. Crushing pancreatic enzymes with enteral feeds in an extremely premature infant with cystic fibrosis—a novel and effective technique. <i>European Journal of Clinical Nutrition</i>. 2021;75(1):214-7. 16. Ng SM, Moore HS. Drug therapies for reducing gastric acidity in people with cystic fibrosis. <i>Cochrane Database of Systematic Reviews</i>. 2021(4). 17. Proesmans M, De Boeck K. Omeprazole, a proton pump inhibitor, improves residual steatorrhea in cystic fibrosis patients treated with high dose pancreatic enzymes. <i>European journal of pediatrics</i>. 2003;162:760-3. 18. Francisco MP, Wagner MH, Sherman JM, Theriaque D, Bowser E, Novak DA. Ranitidine and omeprazole as adjuvant therapy to pancrelipase to improve fat absorption in patients with cystic fibrosis. <i>Journal of pediatric gastroenterology and nutrition</i>. 2002;35(1):79-83.

VERSION/NUMBER	DATE
Original 1.0	22/08/2025
REVIEW	22/08/2030

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Citation for the current version

Bolisetty S, Katz T, Krishnan U, Ooi K, Hall C, Marks K, Dutt S, Jackson R, Azeem MI, Mehta B, Phad N, Barzegar R, O'Grady R, Tran T, Chen C, Brites CC, Knox K, Malloy B, Brew S, van den Boom J, Seigel A, Kwan T, Tian C, Watson E, Gengaroli R, Hassall S, Callander I. Creon (Pancrelipase). Consensus formulary by the Australasian Neonatal Medicines Formulary group. Version 1, dated 22 August 2025. www.anmfonline.org

NEW RELEASE

Appendix. Administration of Creon within the NICU

If infant can swallow and deemed safe to administer PERT via mouth

Step 1	Obtain the prescribed dose using the scoop supplied with the product. Full scoop = 5,000 IU of lipase.
Step 2	Prepare the mix as below at the time of feeding, not in advance.
Step 2	Mix the granules with 1/4 th teaspoon (or just enough to coat the enzyme beads) of apple or pear puree (not juice)
Step 3	Administer the mix orally using a soft tipped infant feeding spoon immediately prior to the feed. if feeding is taking longer than 30 minutes (especially if breastfeeding plus top up bottle) then dose can be split so half is given at the start and half in the middle of the feeding period.
Step 3	Clear gums of residual enzymes using a clean finger and swiping around the gums to make sure no beads are caught in the gums.
Step 4	Consider zinc-based cream to the buttocks and frequent diaper changes to prevent skin excoriation.

Bolus feeds (either via gravity or pump)

Step 1	Obtain the prescribed dose using the scoop supplied with the product. Full scoop = 5,000 IU of lipase.
Step 2	Wearing a mask. Crush the dose of enzyme beads into a powder form using a mortar and pestle or a pill crusher.
Step 3	Add crushed enzyme beads to the feed and swirl the feed.
Step 4	Allow the feed to sit for 20 minutes prior to administration, swirling periodically.
NOTE	If the amount of enzyme needed for 1 feed is too small to crush, 2 or more doses can be crushed together and then divided up into bolus feed doses.

Continuous feeds

Step 1	Obtain the dose required for 2-4 hours' worth of feed depending on unit's policy on hang time (3, 7)
Step 2	Wearing a mask. Crush the 2-4-hour dose of enzyme beads into a powder form using a mortar and pestle or a pill crusher.
Step 3	Add crushed enzyme beads to a 2-4-hour volume of feed and swirl the feed.
Step 4	Allow the formula to sit for 20 minutes prior to infusion, swirling periodically.
Step 5	Feed hang time is 2- 4 hours depending on the unit's policy. The above process must be repeated 2-4 hourly throughout the continuous feeding period.
NOTE	if the amount of enzyme needed for 2- 4 hours' worth of feed is too small to crush, 2 or more doses can be crushed together and then divided up into 2-4 hourly doses

*** Wearing a mask will help to prevent any unwanted inhalation of enzymes during crushing.**