

Pancreatic Enzyme Therapy for Cystic Fibrosis (CF) / Pancreatic Insufficiency (PI)

Disclaimer: Managing or recommending pancreatic enzymes may not be in the scope of practice of all dietitians. Because enzymes are medications, referring to a CF physician, CF nurse practitioner, CF pharmacist or GI physician for prescription advice may be warranted.

How to determine who needs enzymes:

- Fecal Elastase
 - Preferred method to determine need **FOR** enzymes; elastase does **NOT** tell you how well enzymes are working
 - < 100 indicates PI;
 - 100-200 borderline pancreatic insufficient;
 - > 200 normal and should not need enzymes
 - Watery or diluted stool can result in a false positive / low elastase levels (ostomy output, breast milk stool near birth, viral illness)
- 72 Hour Fecal Fat with Diet Diary
 - RARELY done due to complexity in collecting stool and food record for accurate assessment; extremely difficult to do for a child in diapers
 - Once collected, stool analysis takes a week to return result
 - Fat absorbed calculation:
$$\frac{[\text{Grams fat in from diet}] - [\text{Grams fat out from stool per lab report}]}{\text{Grams fat in from diet}}$$

Goal for absorption = > 90% in CF/PI
Healthy normal is 93-100% absorption
- Two CF gene mutations consistent with pancreatic insufficiency (PI)
 - $\Delta F 508$ – most common CF gene associated with pancreatic *insufficiency*
 - $R117H$ – most common gene associated with pancreatic *sufficiency*
 - Many times the newborn screening form contains the CF genes. A physician should interpret the likelihood of pancreatic insufficiency from this information.
- Pancreatic Stimulation Testing during EGD (look for results in lab results in Epic or GI notes)
 - Low levels of lipase, amylase
- Other
 - Pancreatic cancer
 - Complex GI surgeries
 - Complications of chemotherapy / cancer

Common Enzyme Medications:

- Zenpep: Capsule strengths: 3000, 5000, 10,000, 15,000, 20,000, 25,000, 40,000
 - Zenpep is the preferred enzyme for Wisconsin Medicaid patients
- Creon: Capsule strengths: 3000, 6000, 12,000, 24,000, 36,000

- Samples are no longer available in CF clinic. Pharmacy vouchers from the enzyme company or the hospital may be used if no insurance coverage; talk to a social worker or CF dietitian about these options.
- Both Creon and Zenpep are on formulary at CW
 - Not all strengths may be available.
- Other enzymes not on formulary at CW:
 - Pertzye which contains bicarbonate
 - Pancreaze
 - Viokase (non-enteric coated enzyme)
 - RELIZORB (cartridge, used only for enteral nutrition)
 - Note: There is NOT a generic enzyme available
 - Patients may bring these enzymes from home if they choose. Pharmacy will need to be notified.
- Each enzyme capsule contains the amount of lipase listed in the enzyme name:
For Example: Creon 6,000 contains 6,000 units of lipase per capsule

How much enzyme is needed?

- Starting dose for infants with CF is usually 2000-5000 units lipase per feeding or 1000-2000 units lipase/kg/feeding
 - Often kids without CF can have a lower dose than kids with CF and still be successful; giving ~ 1000 units lipase/kg could be a good starting point
 - Infants usually start with one 3000 or 5000/6000 unit capsule per feeding.
 - Dose of enzymes rapidly change in a growing infant; if in doubt, start on low end and increase in 3-7 days
 - Epic does not allow half capsules to be ordered. Check with a pharmacist if a half dose is needed to assure accurate dosing.
- For infants and older children with CF, the usual Children's Wisconsin maintenance dose for enzymes is 1800-2200 units lipase/kg/meal
 - Enzyme doses for snacks are usually half of a meal dose or whatever is closest to giving a full capsule rather than half capsule
- CF Foundation recommends a dose no higher than 2,500 units lipase/kg/meal or no greater than 10,000 units lipase/kg/day
 - Upper limit of 10,000 units lipase/kg/day not applicable to young infants experiencing rapid weight gain

Dosing enzymes for infants

- Enzymes need to be given with human milk and all types of infant formula
- Open the capsule and sprinkle the "beads" on a small (1/2-1) teaspoon of applesauce
- Give the applesauce and "beads" by spoon at the beginning of the feeding
- Wipe away any remaining "beads" that are noticed at the end of the feeding on the child's mouth, skin or mother's breast
- Do not crush or try to dissolve enzymes for oral intake – the coating on the enzymes protects the enzyme from stomach acid
- Repeat dose of enzymes if next feeding is greater than 45 minutes from last enzyme administration

- Use barrier ointments (Bag Balm, Triple Paste, Desitin) when enzyme therapy is starting to prevent diaper rash
- NICU babies with pancreatic insufficiency who have been on TPN usually start enzymes when the oral/enteral intake is ~ 20-30 ml every 3 hours

Enzyme dosing for children and adults

- Give enzymes with each meal and snack that contains fat and/or protein
- Give at the beginning of meal or snack
- If large numbers of capsules, divide between beginning, middle and end of meal
- Enzymes are effective for 45 minutes
- Repeat enzyme dose if meal or snack is longer than 45 minutes than when enzymes were last taken

Increasing Enzymes

- Enzymes need periodic adjustment
 - During times of rapid growth
 - Calculate dose of lipase/kg/meal and increase if not in 1800-2200 units lipase/kg/meal range
 - Infancy
 - Adolescence
 - Development of malabsorption symptoms (constipation needs to be ruled out first)
 - Poor weight gain
 - Lower levels of absorption based on 72 hour fecal fat

Symptoms of Fat Malabsorption

- Large, bulky BMs
- Loose BMs
- Foul-smelling BMs
- Mucous or oily in BMS
- Excessive Gas and/or stomach pain
- Distention or bloating
- Poor weight gain despite good (sometimes ravenous) appetite

Note: Watery diarrhea is NOT on this list

Enzyme Therapy for Tube Feedings

- RELiZORB: FDA approved for 5 years and older. Often used in younger infants/children as well. Considered the standard of care for digestion of tube feedings in the setting of pancreatic insufficiency
 - Enzyme cartridge contains iLipase to hydrolyze fat in formula prior to infusion into feeding tube. RELiZORB is used instead of crushed enzymes.
 - See website, www.RELiZORB.com. Check list of compatible formulas for ideal hydrolysis to use with RELiZORB
 - Not stocked for inpatient use at CW
 - Usually started outpatient in CF clinic
 - Enrollment form / prescription available on the RELiZORB website

- Clinic notes and letter of medical necessity needed at time of enrollment
- Insurance coverage has improved, but the process takes time. Wisconsin Medicaid and Medicaid HMOs provide low reimbursement that often isn't accepted by RELiZORB
- **Crushed Enzymes:** The “beads/microspheres inside a Creon or Zenpep may be crushed. Adding crushed enzymes to formula creates a “predigested” formula prior to infusing into the stomach
 - Families should purchase a mortar and pestle to grind the beads. Generally, a pill crusher will not work, especially with Creon.
 - For inpatient use, the mortar and pestle is accessed through the Med Select system (on W11) or by contacting an inpatient pharmacist. At discharge, the mortar and pestle will be sent home with the patient.
 - The beads are crushed using a circular, rotating movement of the pestle. All beads must be flattened or pulverized into a fine powder. Avoid breathing in the dust from the crushing process.
 - If a family has difficulty crushing Creon, replace tube feeding enzymes with Zenpep in a similar dose. Zenpep crushes much easier.
- This dosing of crushed Creon or Zenpep may be used as an approximate starting point for tube feedings:

Caloric Density of Formula	Amount of Crushed Enzyme per 240 mL
Infant formula 20-27 Cal/oz	1 Creon 6,000 or 1 Zenpep 5,000
1.0 Cal/mL pediatric or adult formula	1 Creon 12,000 or 1 Zenpep 10,000
1.5 Cal/mL pediatric or adult formula	1 ½ Creon 12,000 or 3 Creon 6,000 or 1 Zenpep 15,000
2.0 Cal/mL adult formula	1 Creon 24,000 or 1 Zenpep 20,000 or 25,000

- Mix the crushed enzymes into the entire amount of formula used.
- Allow the enzyme/formula mixture to sit for 15-20 minutes before starting the feeding to allow the enzymes to digest the formula.
- Hang only enough enzyme/formula mixture for a 4 hour infusion in the hospital environment. Refrigerate the remainder, and refill as needed to complete the feeding. Formula and crushed enzymes can be premixed and stored in the refrigerator for up to 24 hours.
- Partially or predigested formulas may require less crushed enzymes.
- If malabsorption is present, a partial dose of enteric coated enzymes may be given at the beginning of the tube feeding to optimize digestion of the first 30-60 minutes while the crushed enzymes are “digesting” the formula.
- It is important that ALL formula be infused for maximum Calorie/nutrient intake.

Foods that don't require Pancreatic Enzymes (however, these food/drinks are generally not going to promote wt. gain.)

- Fruits
- Juice, juice drinks

- Plain vegetables
- Soda or sport drinks
- Pedialyte
- Tea, coffee (without cream)
- Candy without chocolate or nuts (jelly beans, gum drops, hard candy, etc.)
- Fruit snacks
- Popsicles, freezer pops, flavored ice

Nutrition Therapy for Pancreatic Insufficiency

- High Calorie, high protein
- >40% of Calories from fat
- Supplement with fat soluble vitamins
- General Calorie goals are DRI x active / very active
- Protein needs are generally 2 gm/kg
- Persons with CF and pancreatic insufficiency who also receive a highly effective CFTR modulator (Trikafta) may not require as many calories as those not on modulator therapy. Consult a CF dietitian for further assessment.

Vitamin Therapy for Fat Malabsorption

- Fat soluble vitamin deficiency associated with fat malabsorption
- CF specific vitamin supplements designed to provide higher A,D, E, & K levels
 - Drops (MVW Complete Formulation drops used at CW; standard dose is 0.5 mL/day)
 - Chewable tablets (MVW Complete Formulation bubblegum chewable used at CW; standard dose is 1 chewable per day)
 - Softgels (MVW Complete Formulation D3000 softgels used at CW; standard dose is 1-2 softgels per day)
- Take vitamin supplements with a large meal and pancreatic enzymes to optimize absorption