Childhood Acute Illness & Nutrition Network

KEMRI | Wellcome Trust
Clinical Trials

Pancreatic Enzymes and Bile Acids: A Non-Antibiotic approach to Treat Intestinal Dysbiosis in Acutely Ill Severely Malnourished Children

Study Specific Procedure	**SSP No:** CL05 **Version No:** 1.0 **Supersedes:** None **Effective Date:** 19th October 2021

Title: Drug Administration Procedure

	NAME	SIGNATURE	DATE
PREPARER	Johnstone Thitiri		**15th June 2021**
Q.A. AUTHORITY	Aisha Bwika		**16th October 2021**
APPROVING AUTHORITY	Robert Bandsma		**17th October2021**

1.0 PURPOSE / INTRODUCTION:

1.1 PB SAM trial aims to determine safety and effectiveness of pancreatic enzymes and bile acids in treatment of dysbiosis. Dysbiosis is a condition characterised by dislocation of intestinal bacteria from one part of the intestine to another, mainly from the lower part of gut or colon to upper part of the gut i.e. small intestine. This in turn results in inflammation and risk of microbial translocation across the gut resulting in systemic illness and inflammatory process. It is hypothesised that use of bile acids and pancreatic enzymes in malnourished children will treat this dysbiosis and improve clinical outcomes in children with SAM.

1.2 Pancreatic enzyme (and matching placebo) is available in granules packaged in bottles and dispensed using special scoops from manufacturer. Ursodeoxycholic acid (or matching placebo) is available in powder form and packaged in bottles to be reconstituted with water to make an oral suspension.

1.3 Pancreatic enzyme is produced as a biological extract and contains the three known pancreatic enzymes i.e *Proteases* that break down protein, *amylase* that break down carbohydrates and *lipase* that breaks down lipids.

1.4 Ursodeoxycholic acid (UDCA), also known as ursodiol, is a secondary bile acid, produced in humans and most other species from metabolism by intestinal bacteria.

1.5 The purpose of this SSP is train staff on correctly identifying study product, ensuring correct measurement for dispensing and documentation.

2.0 SCOPE / RESPONSIBILITY

2.1 This SSP applies to study clinicians, nurses and pharmacists who will be involved in preparation and dispensing of the investigational products

2.2 The Principal Investigator through the lead clinician retains the overall responsibility of ensuring correct study drugs are given to study participants in a safe and timely way.

3.0 DEFINITIONS

3.1 Scoop: A special spoon-like device provided by manufacturer to be used to measure quantity of pancreatic enzymes granules to be dispensed.

3.2 Pancreatin: Same as pancreatic enzyme

3.3 SAM: Severe acute malnutrition

3.4 IP: Investigational product

4.0 EQUIPMENT / MATERIALS

1. Clean water for reconstitution
2. Study IP

5.0 METHODOLOGY:

5.1 Pancreatin or Placebo:

5.1.1 Presentation

- Pancreatin powder and placebo has been manufactured in Europe by Abbot Pharmaceuticals and custom-packaged for the trial. Each unit is made of a box containing a bottle with 20g of pancreatin or placebo granules.
- The IP has been specifically labelled for the PB SAM trial with study information, Participant numbers, Sponsor and Investigator Information and dosage forms.
- The IP comes with pre-printed study ID numbers found on the label.

5.1.2 Dose calculation

- The dose will be calculated using ***Protease component of the pancreatin powder***, and is set as 3000 IU lipase/kg, twice per day, just prior to a feed. Calculation MUST be made by a trained study clinician.
- This dose translates to (1440 IU/kg amylase and 80 IU/kg protease) which is the dose used for children with cystic fibrosis and exocrine pancreas insufficiency
- For edematous malnutrition participants, weight used for dosing is reduced by a pragmatic 10%.
- Considering dose presentation in scoops, prescription will follow weight bands to allow a lower range of 2000 IU/kg/day and upper range of 4000 IU/kg/day.
- Each scoop contains 5000 IU lipase/kg, the basis for dose calculation in this trial.

Weight (Kg) From	Weight (Kg) To	Dose (scoops)	Dose (IU Lipase)	Upper range (IU/kg/dose)	Lower range (IU/kg/dose)
2.50	4.99	2	10000	4000	2000
5.00	7.49	4	20000	4000	2670
7.50	9.99	6	30000	4000	3000
10.0	15.0	8	40000	4000	2667

- Individuals in the placebo group will receive placebo using the same weight-based dosing according to dosing scheme table above.
- After dose calculation using the table above, the number of scoops for each child will

be written on the box using a marker pen.

5.1.3 Pancreatin dispensing

- Pancreatin granules is to be dispensed twice in a day. Best preferable times are 9am in the morning and 9 pm at night.
- The dose is required to be taken continuously while in hospital and at home for a total of 21 days.
- Study nurses, clinicians and field workers should assist the carer of the child with dispensing while in hospital. This should result in confidence by carer to dispense alone when the child is discharged home from hospital. Refer to the training SOP for mothers on dispensing of investigational products.
- Pancreatin granules can be dispensed to a child in two ways;
  1. Sprinkle over food –
     a. Take a small amount of food meant for the child. Separate a small portion that the mother is sure the child will complete
     b. Sprinkle the granules over this portion. Do not mix.
     c. Give the child this food over the next 10 minutes and ensure all food is given.
     d. If child vomits food, DO NOT REPEAT DOSE
  2. Mix with milk
     a. Take a small volume of milk, about 10 teaspoons and pour into a feeding cup
     b. Add the required number of scoops of Pancreatin granules into the milk and stir.
     c. Whirl around and wait for 3 minutes to dissolve.
     d. Give the milk to the child.
     e. Confirm no sediments of the granules remain settled at the bottom of the cup. If any, add some more milk, swirl the cup around to help in dissolution and give child.
- Pancreatin may also be given by NG- tube for children who are ill and are feeding by this tube. Use the meal being provided to child e.g. F75 milk to mix with the granules.

5.2 Ursodeoxycholic acid or Placebo:

5.2.1 Presentation

- This has been manufactured by Asian Manufacturer – Opsonin Pharma and custom-packaged for the trial in bottles.
- Ursodeoxycholic acid is available in form of a syrup. Each bottle contains 50mls of study drug.

5.2.2 Dose calculation

- The dose of Ursodeoxycholic acid will be 10 mg/kg twice per day just prior to a feed, using a suspension of 50 mg/ml.
- For oedematous malnutrition participants, weight is pragmatically reduced by 10%.
- A weight-based dosing scheme will be used to guide calculation of doses for both ursodeoxycholic acid and placebo. This is shown in the table below.

Weight (Kg) From	Weight (Kg) To	Dose (ml)	Dose (mg)	Upper range (mg/kg/dose)	Lower range (mg/kg/dose)
2.50	3.99	0.6	30	12.0	7.5
4.00	5.99	1.0	50	12.5	8.3
6.00	7.99	1.4	70	11.7	8.7
8.00	9.99	1.6	90	11.3	9.0
10.0	15.0	2.2	110	11.0	7.3

5.2.3 Dispensing of Ursodeoxycholic acid

- Dispense the calculated dose of Urso using a syringe. Given that the volume bracket for children upto 15 kgs range between 0.6mls and 2.2 mls, use smaller volume syringes to draw the syrup due to better graduations or accuracy. E.g. 2ml syringes for doses below 2mls, and 5ml syringes for doses above 2mls.
- A syringe should be used only once to avoid risk of contamination.
- Insert the syringe into the child's mouth and allow child to suck slowly until all is used. Discard the syringe.
- Train mothers while in the ward on use of syringes and dispensing.
- In case of spillage, or spitting by child, do not repeat dosage .

6.0 APPENDICES

None

7.0 REFERENCES:

None

8.0 DOCUMENT CHANGE HISTORY

Version Table:

Version 1.0: Title: **Drug Administration Procedure**	Dated: **19th October 2021**	SSP No.: **CL05**	No. Pages: **7**
Version 2.0: Title:	Dated:	SSP No.:	No. Pages:
Version 3.0: Title:	Dated:	SSP No.:	No. Pages:
This document is effective from the date of training/last approval signature and will be reviewed in two years.			

SSP Review and Updating Logs

DATE	NAME OF REVIEWER	SIGNATURE	REASON FOR REVIEW AND CHANGES MADE

SOP AWARENESS LOG

I, the undersigned below, hereby confirm that I am aware that the accompanying SSP is in existence from the date stated herein and that I shall keep abreast with the current and subsequent SSP versions in fulfilment of Good Clinical Practice (GCP).

Number	Name	Signature	Date (dd/mmm/yyyy)
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