Royal Hospital for Women (RHW)
NEONATAL BUSINESS RULE
COVER SHEET

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SUMMARY	To provide feeding guidelines for preterm neonates with birth weight ≤1000g

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Enteral Nutrition - Preterm infants 1000g and under — RHW CLIN015

1. BACKGROUND

This CBR provides feeding guidelines for preterm neonates with birth weight ≤1000g. The recommended nutritional practice for very low birthweight infants is to provide mother's own milk (MOM) along with a human milk fortifier (HMF) to avoid protein and nutrient deficiencies.

2. RESPONSIBILITIES

Medical, Nursing and Allied Health Staff

3. PROCEDURE

3.1 Nutrition Goals

- Regain birthweight by 10-14 days of age.[1]
- Achieve physical growth targets in the NICU [2]
  - Weight – 21 g/kg/day (±2 g/kg/day)
    - Weight gain may slow to 25-30g/day as approaches 40 weeks CGA.
  - Length – 1.1 cm/week (±0.2 cm)
  - HC target – 1.1 cm/week (±0.2 cm)
- Minimise the risk of necrotising enterocolitis.
- Prevent osteopenia of prematurity
- Improve neurodevelopmental outcomes.

3.2 Clinical Practice

<u>Prior to birth</u>

- Antenatal counselling: NICU medical team or CMC for lactation to provide counselling for the woman and her partner about the importance of expression of mother's own milk, breastfeeding, feeding goals, availability of pasteurised donor human milk (PDHM) Humavant (Human Milk Derived Fortifier) and probiotic. But DO NOT encourage expression prior to delivery, which may facilitate preterm labour.
- Consent: Obtain written informed consent for PDHM, Humavant and probiotic.

<u>At birth</u>

- Commence trophic gavage feeding 1 mL MOM or PDHM 2 hourly and continue for 48 hours as tolerated. First feed to be administered within 6 hours of life.
- Commence probiotic within 6 hours of life.

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After 48 hours of life – Grading up feeds

- Continue 2 hourly bolus feeds.
- Increase feeds until 170-180 mL/kg/day is reached.

Current Weight	Rate of increase	
	If 2 hourly bolus feeds	If hourly bolus feeds
<500g	0.5 mL per feed per 24 hours	0.3 mL per feed per 24 hours
500 – 700g	1 mL per feed per 24 hours	0.5 mL per feed per 24 hours
701 – 1000g	1 mL per feed per 12 hours	0.5 mL per feed per 12 hours

  - Grading up feeds may need to be slow or altered (eg. hourly bolus feeds, slow bolus feeds over 20-30 minutes, continuous feeds, transpyloric feeds) in special circumstances, such as:
    - Growth restriction
    - Abnormal umbilical Doppler's
    - Feed intolerance
    - Necrotising enterocolitis and other medical or surgical gastrointestinal conditions
    - Haemodynamically significant PDA (particularly infants on indomethacin or ibuprofen)
    - Infants on inotropic support and/or muscle relaxants
  - If continuous enteral feed is chosen – draw up only 2-hour feed volume into syringe and administer it using an infusion pump. Feed should be agitated gently every 1 hour to avoid sedimentation.
- Consider changing frequency of feeds to 3rd hourly once the infant is ≥1500g.

NOTE:
- Some infants may tolerate 2nd or 3rd hourly feeds a lot earlier than these guidelines and NICU team may decide to change the feed intervals as appropriate for these infants.

Fortification

- If consented for Humavant (preferred option)
  - Commence Humavant+6 when 80-120 mL/kg/day of enteral feeds are commenced.
  - Continue Humavant fortification until 33+6 weeks corrected gestational age**.
  - At 34+0 weeks corrected gestational age, transition to cow's milk-based fortifier (CMBF) as detailed in Humavant policy (Appendix 3).
  - After transition to CMBF, if infant remains on PDHM transition to preterm formula or alternate formula as prescribed by neonatal team as per PDHM guideline.
  - Continue CBMF fortification until the time of discharge and or until transitioning to breast feeds.

NOTE:
- Humavant Cream CR may be prescribed for some infants from ≥120 mL/kg/day to achieve adequate weight gain (Appendix 3).
- Do not use Beneprotein or MCT when using Humavant.
- Humavant +8 may be needed if:
  - fluid restricted to <160ml/kg/day.
  - poor growth velocity on Humavant +6 at optimised volumes and low blood urea nitrogen.
- **Some infants may need to transition to cow's milk-based fortifier earlier (at 32 weeks CGA) if planned for transfer to another hospital.

- If not consented for Humavant use CMBF
  - Commence half fortification (22-23 kcal/30ml; 73-76kcal/100ml) when enteral feeds reach 100-120 ml/kg/day and full fortification (24-25 kcal/30ml; 80-83kcal/100ml) at 120-150 mL/kg/day of enteral feeds.
  - If standard fortifier is not tolerated or extra protein or calorie required, NICU dietitian and team may opt to use Beneprotein and/or MCT oil.

Transitioning from parenteral nutrition (PN)

- Change to **concentrated** preterm PN once the standard preterm PN volume is <100 mL/kg/day.
  - Maximum **concentrated** preterm PN solution should not exceed 100 mL/kg/day.
  - Volume >100 mL/kg/day requires approval from neonatologist/NICU dietitian.
  - Maximum **standard** preterm PN solution that can be given is 135 mL/kg/day.
- Cease intravenous lipid emulsion once the infant tolerates 120 mL/kg/day of enteral feed.
- Cease preterm PN solution and remove central line once the infant tolerates 150 mL/kg/day of enteral feeds.

Multivitamins and Iron supplementation

- With Humavant
  - Add Multivitamin the day after SMOF lipid ceased.
    - Pentavite 0.45 mL daily OR
    - Brauer 0.5ml twice per day + vitamin D 400IU daily
  - Add Iron 2 mg/kg/day at full feeds after 2 weeks of life.
- Without Humavant
  - Add Multivitamin the day after SMOF lipid ceased.
    - Pentavite 0.45 mL daily OR
    - Brauer 0.5ml twice per day + vitamin D 400IU daily
  - Iron is not required if PreNaN CMBF is used at >160mL/kg/day.

Monitoring

- Clinical monitoring for feed intolerance
  - Medical team to assess the abdomen once a shift or more frequently if concerns of abnormal findings such as abdominal distension, discolouration or blood in stool.
  - Prefeed gastric aspirate to confirm the IGT position: Aspirate only up to 0.5 mL to check the colour of aspirate and the pH for tube position.
    DO NOT ROUTINELY ASPIRATE THE ENTIRE GASTRIC RESIDUALS (GR).
  - If aspirate/vomit is heavily bile stained (colour number 7 or 8 (Figure 1) – return the aspirate, stop feeds and notify medical team for assessment.
  - Occasionally, the volume of aspirate would be measured.
    - If aspirate volume is <50% of previous 6-hour volume, not heavily bile stained and clinically stable abdomen, return aspirate and continue to feed.
    - If aspirate volume ≥50% of previous 6-hour volume or heavily bile stained, return aspirate, stop feed and assess the infant for any abdominal pathologies.

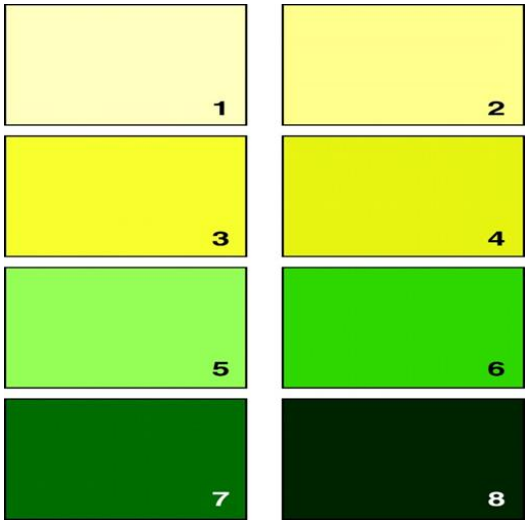

Figure 1

- Growth
  - Weight every Monday, Wednesday and Friday.
    - Weight target 21 g/kg/day (±2 g/kg/day)
      - Weight gain may slow to 25-30g/day as approaches 40 weeks CGA.
  - Length and head circumference every Wednesday.
    - Length and head circumference target 1.1 cm/week (±0.2 cm)
- Biochemical markers
  - Weekly urine Calcium (Ca) and Phosphorus (P) (Sunday night)
    - Aim for urine Ca and P of 1-2 mmoL/L.[3, 4] This is a surrogate marker of an adequate intake of Ca and P with a slight surplus.
    - If too much of Ca (>2 mmol/L) and P (>2 mmol/L) in the urine it may need further intake/output assessment to rule out excess intakes or excess excretion.
  - Weekly/Fortnightly serum Ca/Mg/P/urea/Cr, Liver function test and vitamins
    - Blood urea nitrogen of 3.2-5 mmoL/L is a surrogate marker of adequate protein intake.[26-27] However, aiming that range of BUN may mean excess protein intakes in daily practice. Consult with NICU dietitian to individualise the protein intakes.
    - Serum P <1.6 mmoL/L is considered as hypophosphataemia.[5]
    - Serum Vitamin A, D, E, K and folate until transitions from Humavant to CMBF.

3.3 Educational Notes

- The recommended nutritional practice for very low birthweight infants is to provide their own mother's human milk along with a human milk fortifier (HMF) to avoid protein and nutrient deficiencies.[1]
- A 2021 Systematic review and meta-analysis included 2 RCTs3, 4 with a total of 334 infants<1250g. This review found that human milk-based fortifier compared with cow's milk-based fortifier reduced the risk of necrotising enterocolitis (risk ratio 0.47, 95% CI 0.22 to 0.98) but the overall quality of evidence was low.[6] (LOE I, GOE C)
- A 2017 systematic review summarised the evidence regarding the association of donor human milk, exclusive human milk diet and different human milk doses with incidence of NEC in preterm infants. This review found consistent evidence that a higher dose of mother's own milk (at least

50%) reduces the risk of NEC. There is preliminary evidence that an exclusive human milk diet may provide protection against NEC.[7]

- In extremely low birthweight infants, use of an exclusively human milk diet (i.e. mother's milk or donor human milk plus a human milk-derived fortifier) has also been reported to result in: (1) decreased length of hospital stay and cost, (2) reduction of parenteral nutrition days, (3) reduced days of feeding intolerance and number of days to full feeds,3 (4) improved weight and length velocity, (5) lower mortality, (6) reduced incidence of late onset sepsis, (7) and reduced incidence of retinopathy of prematurity and chronic lung disease, but there are several limitations in these studies.[8-18]
- These local guidelines are a compilation of an integrated system for providing optimal newborn care, family integrated care, kangaroo care (skin-to-skin contact), rooming-in, respecting the WHO/UNICEF Ten Steps to Successful Breast-feeding expanded in 2011 for use in NICUs, and other best practices for neonatal care.[19-20]
- This feeding strategy aims to promote and support breastfeeding in the NICU.
- Early intervention with milk expression soon after delivery (ideally within 1 hour of birth) is critical for milk production of NICU mothers; therefore, mothers should be taught a method of milk expression within this time frame.
- This feeding strategy should be done in conjunction with Immuno-Supportive Oral Care (ISOC).[20]
- Regaining birthweight: Initial weight loss of 7%–10% is expected, reaching a nadir at days 3–4, nutritional strategies should aim to regain birth weight by 7–10 days of age. Nutritional management and growth assessment for SGA infants should be the same as those born AGA, but initial weight loss is often less and acceptable up to 4%–7% of birth weight.[1] It is to be noted that, in Ehrenkranz RA et al study, the "highest growth velocity during the NICU stay" group took significantly longer to regain birthweight (average 19 days) compared to lowest growth velocity group in their cohort (average 16 days).[2]
- Advancement of feeds: A 2021 Cochrane review concluded that advancing enteral feed volumes at increments of 30 to 40 mL/kg/day (compared to 15 to 24 mL/kg/day) does not increase the risk of NEC or death in VLBW infants (<1500g). This review found that advancing the volume of enteral feeds at slow rates results in delay in establishing full enteral feeds (on average 3 days extra in the largest trial in the meta-analysis) and may slightly increase the risk of invasive infection (RR 1.14, 95% CI 0.99 to 1.31; RD 0.02,95% CI −0.00 to 0.05; certainty of evidence is low). Applicability of these findings to extremely preterm, extremely low birth weight, or growth-restricted infants is uncertain, although authors suggested the findings can be extrapolated to ELBW infants.[28]. A 2022 systematic review on fast feed advancement (≥30 ml/kg per day) compared with slow feed advancement (<30 ml/kg per day) in preterm (<37 weeks) and low birth weight infants (<2.5 kg) found that fast feed advancement reduces time to regain birth weight and likely reduces the length of hospital stay; it also likely reduces the risk of neonatal morbidity and mortality slightly. However, it may increase the risk of neurodevelopmental disability slightly. This meta-analysis included 12 RCTs with 4291 participants. This meta-analysis did not provide any subgroup analysis for ELBW infants (<1000g).[30] The Ireland Speed of Increasing Milk Feeds trial (SIFT) was the largest trial (n = 2804). Among 2804 infants, SIFT trial included 1020 extremely low-birth-weight infants (<1000 g), 994 extremely preterm infants (<28 weeks of gestation), and 435 infants with absent or reversed end-diastolic umbilical flow on antenatal Doppler studies. In this large, pragmatic, randomized, controlled trial, advancing milk feeding volumes at daily increments of 30 ml per kilogram as compared with 18 ml per kilogram did not affect survival without moderate or severe neurodevelopmental disability at 24 months, corrected for gestational

age. The speed of increment in feeding volumes also did not affect the risks of late-onset sepsis, necrotizing enterocolitis, or death during hospitalization. However secondary-outcome analysis showed the risk of moderate or severe motor impairment was higher in the faster-increment group.[29]

- The most recent evidence from the SIFT study showed that slow advancement of feeding in very low birthweight infants did not reduce the risk of NEC showing no advantage in increasing at 18ml/kg/day versus 30ml/kg/day.[29]
- Routine prefeed gastric residual (GR) aspiration of entire contents in the clinically stable infant is not recommended. Assessment of GR volumes should be performed only when other clinical signs associated with feed intolerance or NEC are present.[1]
- Bolus feeds promote cyclical release of gastrointestinal tract hormones to stimulate gut maturation and motility but marked variations in practice exist and many use continuous feeds. Low-quality evidence suggests feeding 3-hourly is comparable to 2-hourly feeding although extremely low-birth-weight infants may reach full enteral feeds earlier when fed 2-hourly compared with 3-hourly. Bolus feeding increases splanchnic perfusion more than continuous feeding. Energy expenditure may increase upon bolus feeding as compared to continuous feeding. Systematic reviews show longer time to reach full enteral feeding using continuous rather than intermittent feeding infants[21] and fat loss may also be greater although there were no significant effects on growth. Data on apnoea are inconsistent.[1] In our guideline, fat loss and sediment formation will be mitigated by limiting the continuous feed volume to not more than 2-hour volume, meaning milk is prepared every 2 hours and infusion syringe and pump are placed vertically.
- Growth targets of weight - 21 g/kg/day (±2 g/kg/day), length and HC target: 1.1 cm/week (±0.2 cm) during NICU stay were associated with less likelihood of cerebral palsy, Bayley's mental developmental index (MDI) and psychomotor developmental index (PDI) <70 and neurodevelopmental impairment. Also, these growth targets showed better weight, length and HC at 18-22 months CGA.[2] These growth targets also matched with intrauterine growth[22] and maintain the birth percentile in extra uterine life. (Hypothetical growth charts on eRIC created by C Brites, RHW eRIC senior analyst)
- Growth curves: For preterm AGA infants, maintain the rate/velocity of growth that will achieve and maintain the birth percentile for the infant's birth weight. If the birth percentiles for weight or length are exceeded, consider decreasing nutrient intake. For SGA infants, similarly, maintain daily growth charts and at a minimum maintain the birth percentile for a given birth weight. In SGA infants, achieving the tenth percentile for weight for a given postconceptional age by increasing nutrient intake is a reasonable end point at this time, assuming head growth will follow.[1,23]
- Urine Calcium and Phosphate**:** Preterm infants have been shown to achieve fetal bone mineral accretion rate by maintaining a simultaneous slight excretion of Ca and P in urine (urine concentrations of 1-2 mmoL/L). A large international cohort study demonstrated that regular measurement of urinary Ca and P a valuable and easy means of adjusting Ca and P intake.[3,4]
- Beneprotein is 100% whey protein isolate. It's PDCAAS (Protein Digestibility Corrected Amino Acid Score): 100. Osmolality is 44 mOsm/kg water.

3.4 Abbreviations

MOM	Mother's Own Milk	HMF	Human Milk Fortifier

NICU	Neonatal Intensive Care Unit	PDA	Patent Ductus Arteriosus
PN	Parenteral Nutrition	CMBF	Cow's Milk Based Fortifier
SMOF lipid	Soybean oil, medium-chain triglyceride, olive oil, fish oil	IGT	Intra Gastric Tube
GR	Gastric residue	Ca	Calcium
P	Phosphorus	Mg	Magnesium
Cr	Creatinine	BUN	Blood Urea Nitrogen

3.5 References

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4. RELATED BUSINESS RULES AND POLICY DOCUMENTS

- RHW NCC Medical CBR – Pasteurised Donor Human Milk (PDHM) for vulnerable infants - Refer to DOH PD2018_043
- RHW NCC Medical CBR – Enteral Nutrition - formula preparations in Newborn Care Centre
- RHW NCC Medical CBR – Enteral Nutrition - human milk fortification - preparation
- RHW NCC Nursing CBR – Breastfeeding - First Expression - Refer to CBRs Lactation/Infant Feeding topic
- RHW NCC Nursing CBR – Enteral Feed Warming – Calesca
- RHW NCC Nursing CBR – Immuno-Supportive Oral Care (ISOC)

5. CULTURAL SUPPORT

- When clinical risks are identified for an Aboriginal family, they may require additional supports. This may include Aboriginal health professionals such as Aboriginal liaison officers, health workers or other culturally specific services.
- For a Culturally and Linguistically Diverse CALD family, notify the nominated cross-cultural health worker during Monday to Friday business hours.
- If the family is from a non-English speaking background, call the interpreter service: NSW Ministry of Health Policy Directive PD2017_044-Interpreters Standard Procedures for Working with Health Care Interpreters.

6. IMPLEMENTATION PLAN

This revised CBR will be distributed to all medical, nursing and midwifery staff via @health email. The CBR will be discussed at ward meetings, education and patient quality and safety meetings. Education will occur through in-services, open forum and local ward implementation strategies to address changes to practice. The staff are asked to respond to an email or sign an audit sheet in their clinical area to acknowledge they have read and understood the revised CBR. The CBR will be uploaded to the CBR tab on the intranet and staff are informed how to access.

7. RISK RATING

- High

8. NATIONAL STANDARDS

- Standard 1 Clinical Governance
- Standard 2 Partnering with Consumers
- Standard 3 Preventing and Controlling Infections
- Standard 4 Medication Safety

- Standard 5 Comprehensive Care
- Standard 6 Communicating for Safety

9. REVISION AND APPROVAL HISTORY

Date	Revision No.	Author and Approval
2010	1	S Bolisetty (lead clinician)l; Newborn Care Management Committee and RHW Quality & Patient safety
2018	2	S Bolisetty (lead clinician); NCC LOPs Committee
2019	3	S Bolisetty (lead clinician); NCC LOPs Committee
2023	4	S Bolisetty (Medical Co-Director), S Allworth (Dietitian), E Jozsa (CNS), Madeleine O-Connor (Acting CMC), A Scott-Murphy (NUM), R Jackson (NE), P Everitt (CMC), K Lindrea (CNC), T Parmar (NICU fellow), S Tapawan (NICU CMO), Eloise Deibe (CNE); NCC CBR Committee
21/12/23	4	Endorsed at RHW Safety and Quality Committee
20/05/2024	5	Endorsed BRGC

Appendix 1 - Humavant - Human milk derived fortifier

Parent Information and Consent Form

Dear Parents
We sincerely appreciate that you read this information during this stressful time. We hope this information assists you in making an informed decision regarding the use of Humavant as a fortifier to breastmilk for your baby.

What is human milk fortifier (HMF)?

Breastmilk is the best for your baby. However, breastmilk alone is not sufficient for the optimal growth of a premature baby. This is because she/he needs more energy, protein, vitamins, minerals and salts by her/his rapidly growing body. Adding a food supplement, called human milk fortifier (commonly known as HMF), to the breast milk, provides all additional elements for growth. It is a standard clinical care among the newborn intensive care units (NICUs) that HMF is added to breast milk for babies born with a weight under 1800g.

What are the types of HMF?

There are 2 types of HMF preparations in Australia. One is cow's milk based HMF, which has been used for decades.

As of July 2023, we have a second type of fortifier called Humavant (supplied by Prolacta Bioscience, USA) which is derived from pasteurised donor human milk.
Donors are screened for viruses, illicit drugs and nicotine as well as for other types of infection.
Humavant is an approved food supplement for special medical purpose as per Food Standards Australia New Zealand (FSANZ). It is a registered product in New South Wales.

Are there any benefits of human milk derived HMF over cow's milk derived HMF?

A recent scientific review compiled the studies that compared the exclusive human milk diet (i.e. human milk plus Humavant) with traditional diet containing cow's milk-based products in over 300 preterm infants. The use of exclusive human milk diet reduced the incidence of necrotizing enterocolitis (NEC), a life-threatening gut condition in preterm infants, by half.

Are there any side effects to human milk based HMF?

Human milk derived HMF was shown to be well tolerated. There is no data on long term side effects and no other known risks associated with this product. Despite all the safety precautions, there remains a small chance that an infectious agent may nevertheless be transmitted to your baby or that your baby may not tolerate Humavant or may have a currently unforeseeable reaction to the products.

There is alternative cow's milk derived HMF products available if you wish to avoid Humavant.

Please feel free to discuss with the consultant neonatologist or fellow to provide you with more information if needed. Thank you for your time and consideration.

Appendix 2 - Humavant - Human milk derived fortifier

PARENT CONSENT FORM

I, _____, have received the information provided in the parent information leaflet about Humavant as a fortifier to breast milk for my baby. I have been given enough time to read it and have had the opportunity to ask any questions I want from the staff caring for my baby and all my questions have been answered.

I wish my baby, _____ to receive Humavant, as a fortifier to breastmilk. I understand that Humavant may be added to my baby's feeds. I also understand that clinicians may decide to cease the supplementation if any concerns on its usage for my baby. I understand Humavant is registered as a food product in Australia. I also understand there may be risks with Humavant which are not presently known. I understand that information on my baby's progress may be collected from the hospital notes for audit in future, but that my baby's identity will not be disclosed. I understand that I may request that my baby stop receiving Humavant at any time, without giving a reason.

I have no objection to being contacted in future for the purposes of follow up information. (Delete if not applicable)

Signature of parent/guardian: ……Date: ____/____/____

I have explained the information in the parent information leaflet to this parent:

Name of person obtaining consent: ……..…

Signature of person obtaining consent: ……Date: ____/____/____

Name of interpreter: ……

Signature of interpreter: …….. Date: ____/____/____

Royal Hospital for Women (RHW)
NEONATAL BUSINESS RULE

Enteral Nutrition - Preterm infants 1000g and under — RHW CLIN015

Appendix 3 – Humavant -Human milk fortifier

Alert	Food for Special Medical Purpose as per Food Standards Australia New Zealand (FSANZ) Imported from USA and registered in New South Wales. Obtain written informed consent from parents prior to commencement.
Indication	Nutritional supplement for preterm infants ≤1000 g
Action	Human milk derived fortifier (made exclusively from 100% donor breastmilk) that can be added to mother's milk or donor milk to optimise nutrient content.
Trade Name	Humavant+6 H^2MF Humavant+8 H^2MF Humavant Cream CR
Presentation	**Humavant+6 H^2MF** - comes frozen in 125 mL bottle containing 15mL or 30 mL of fortifier. Provides **27 kcal/30 mL (90 kcal/100 mL)** when 35ml or 70 mL of preterm human milk is added (Mixing ratio 7:3). **Humavant+8 H^2MF** - comes frozen in 125 mL bottle containing 40 mL of fortifier. Provides **29kcal/30 mL (95 kcal/100 mL)** when 60 mL of preterm human milk is added (Mixing ratio 3:2). Humavant Cream CR – comes in 30ml bottle containing 10 mL of frozen caloric fortifier delivering **2.6kcal/mL**
Dosage	**Preterm infants with birthweight ≤1000 g** 1. Commence Humavant+6 H^2MF (27 kcal/30mL preparation) at 80-120 mL/kg/day of expressed human milk/PDHM feed volume. 2. Continue increasing volume to 170-180mL/kg/day and remain on same until 33+6** weeks corrected gestational age. 3. In some infants, Humavant Cream CR may be prescribed from 120 mL/kg/day to achieve adequate weight gain 4. In some infants, Humavant +8 may be needed to achieve adequate nutritional intake and growth.

Dosage and progression up to 33+6 weeks GA	Start when enteral feed	Caloric intake
Humavant+6 H^2MF	80-120mL/kg/day	27kcal/30mL (90kcal/100ml)
Humavant+8 H^2MF	If extra calorie required	29kcal/30mL (95kcal/100ml)

5. At 34+0** weeks corrected gestational age, may transition to cow's milk based fortifier (CMBF) as detailed in the table below.
   **Some infants may need to transition to cow's milk based fortifier earlier (at 32weeks CGA) if planned for transfer to another hospital.

Transition from 34+0 weeks GA
from Human Milk Based Fortifier (HMDF) to Cow's Milk Based Fortifier(CMBF) on 2 hour feed

	Feed 1	Feed 2	Feed 3	Feed 4	Feed 5	Feed 6	Feed 7	Feed 8	Feed 9	Feed 10	Feed 11	Feed 12
Day 0 (33+6)	HMDF	HMDF	HMDF	HMDF	HMDF	HMDF	HMDF	HMDF	HMDF	HMDF	HMDF	HMDF
Day 1 (34+0)	CMBF	HMDF	HMDF	HMDF	CMBF	HMDF	HMDF	HMDF	CMBF	HMDF	HMDF	HMDF
Day 2	CMBF	HMDF	CMBF	HMDF	CMBF	HMDF	CMBF	HMDF	CMBF	HMDF	CMBF	HMDF
Day 3	CMBF	CMBF	CMBF	HMDF	CMBF	CMBF	CMBF	HMDF	CMBF	CMBF	CMBF	HMDF
Day 4	CMBF	CMBF	CMBF	CMBF	CMBF	CMBF	CMBF	CMBF	CMBF	CMBF	CMBF	CMBF

	Transition from 34+0 weeks GA from Human Milk Based Fortifier (HMDF) to Cow's Milk Based Fortifier(CMBF) on 3 hour feed

	Feed 1	Feed 2	Feed 3	Feed 4	Feed 5	Feed 6	Feed 7	Feed 8
Day 0 (33+6)	HMDF	HMDF	HMDF	HMDF	HMDF	HMDF	HMDF	HMDF
Day 1 (34+0)	CMBF	HMDF	HMDF	HMDF	CMBF	HMDF	HMDF	HMDF
Day 2	CMBF	HMDF	CMBF	HMDF	CMBF	HMDF	CMBF	HMDF
Day 3	CMBF	CMBF	CMBF	HMDF	CMBF	CMBF	CMBF	HMDF
Day 4	CMBF	CMBF	CMBF	CMBF	CMBF	CMBF	CMBF	CMBF

6. After transition to CMBF, if infant remains on PDHM transition to preterm or alternate formula as prescribed by neonatal team highlighted in PDHM guideline.

Route

Intragastric tube feedings

Preparation

1. Select correct humavant preparation based on feeding order.
2. Thaw Humavant fortifier in Calesca milk warmer.
3. Using aseptic technique, add EHM/PDHM to thawed fortifier as indicated below:

a. **Humavant+6 H²MF**

i. **50ml preparation:** Add 35mL of EBM/PDHM to 15mL of thawed bottle of fortifier to make a 27kcal/30mL solution (90kcal/100mL).

ii. **100ml preparation:** Add 70mL of EBM/PDHM to 30ml of thawed bottle of fortifier to make a 27kcal/30mL solution (90kcal/100mL).

b. **Humavant+8 H²MF**

Add 60mL of EHM/PDHM to 40mL of thawed bottle of fortifier to make a 29kcal/30mL solution (95kcal/100mL).

c. Humavant Cream CR

Add thawed Cream CR to EHM/PDHM + Humavant mixture (as prescribed by NICU team/dietitian as per below recipes)

Feed order	Nutrition Composition		Recipe			
	Kcal/100ml	Kcal/30ml	Humavant (mL)	EBM / PDHM (mL)	Cream CR (mL)	Final volume (mL)
EBM/PDHM + Humavant +6	90	27	15	35	0	50
+ Cream CR 5kcal	95	29			2	52
+ Cream CR 10kcal	100	31			4	54
EBM/PDHM + Humavant +6	90	27	30	70	0	100
+ Cream CR 5kcal	95	29			4	104
+ Cream CR 10kcal	100	31			8	108
EBM/PDHM + Humavant +8	95	29	40	60	0	100
+ Cream CR 5kcal	100	31			4	104
+ Cream CR 10kcal	105	33			8	108

	4. Gently swirl bottle to mix; DO NOT SHAKE. 5. Measure out the fortified milk using sterile syringes according to the feeding order. 6. Label each syringe with EBM/PDHM and patient identifier label and refrigerate (2°C to 8°C) until administered. **7.** Administer within 24 hours from the beginning of thawing process.
Administration	Warm fortified human milk in milk warmer and administer via intragastric tube
Monitoring	Watch for feeding intolerance
Contraindications	Any condition in which enteral feeding is contraindicated.
Precautions	None
Adverse Reactions	Increased gastric residuals, abdominal distension, vomiting.
Compatibility	Not applicable.
Incompatibility	Not applicable.
Stability	2-year shelf life for frozen product. Administer within 24 hours from the beginning of thawing process.
Storage	Store at -20°C Do not refreeze. Keep thawed product refrigerated until used at 2°C to 8°C (for no more than 24 hours, then discard)
Special Comments	Humavant is made from 100% donor breast milk. The product is a concentrated, pasteurised liquid. Ingredients include human milk and less than 2% of the following: calcium glycerophosphate, calcium gluconate, sodium citrate, magnesium phosphate, calcium chloride, potassium citrate, sodium chloride, zinc sulphate, cupric sulphate.
Evidence	The recommended nutritional practice for very low birthweight infants (<1500 g) is to provide their own mother's human milk along with a human milk fortifier (commonly known as HMF) to avoid protein and nutrient deficiencies.[1] A 2021 Systematic review and meta-analysis[2] included 2 RCTs[3,4] with a total of 334 infants<1250g. This review found that human milk-based fortifier compared with cow's milk-based fortifier reduced the risk of necrotising enterocolitis (risk ratio 0.47, 95% CI 0.22 to 0.98) but the overall quality of evidence was low. (LOE I, GOE C). In extremely low birthweight infants, use of an exclusively human milk diet (i.e. mother's milk or donor human milk plus a human milk-derived fortifier) has also been reported to result in: (1) decreased length of hospital stay and cost,[5,6,13], (2) reduction of parenteral nutrition days,[7,8] (3) reduced days of feeding intolerance and number of days to full feeds,[3] (4) improved weight and length velocity,[9,10] (5) lower mortality,[11,12] (6) reduced incidence of late onset sepsis,[3,12] (7) and reduced incidence of retinopathy of prematurity and chronic lung disease[3,12], but there are several limitations in these studies.
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Appendix 4 - Nutrient estimates of human milk with Humavant+6 H²MF

Nutrients Units/kg/day	ESPGHAN 2022 Consensus	Preterm Human milk per 100 mL[14,15]*	Humavant+6 H²MF		Pentavite 0.45ml + Iron 2mg/kg	Brauer 1ml + Iron 2mg/kg
			per 100mL	180mL/kg		
Osmolality, mOsm/kg			374	374		
Energy (kcal)	115-140(-160)	67	91	163		
Protein (g)	3.5-4.0 (-4.5)	1.1	2.57	4.6		
Fat (g)	4.0-8.1	3.5	5.4	9.6		
Carbohydrate (g)	11-15 (-17)	6.7	7.4	13		
Sodium (mmoL)	3.0-5.0	1.2	2.9	5.3		
Chloride (mmoL)	3.0-5.0	1.6	2.9	5.3		
Potassium (mmoL)	2.3-4.6	1.3	2.4	4.3		
Calcium (mmoL)	3.0-5.0	0.6	3.1	5.6		
Phosphate (mmoL)	2.2-3.7	0.5	2.2	4		
Magnesium (mmoL)	0.4-0.5	0.14	0.37	0.66		
Iron (mg)	2.0-3.0 (-6.0)	0.1	0.1	0.18	2.18	2.18
Zinc (mg)	2.0-3.0	0.4	1.5	2.7		
Copper (µg)	120-230	38	116	208		
Selenium (µg)	7-10	2.4	4.5	8.1		
Manganese (µg)	1-15	0.4	5.8	10.4		
Iodine (µg)	11-55	18	20	35		
Vitamin B1 Thiamine (µg)	140-290	8.9	8	14	555	126
Vitamin B2 Riboflavin (µg)	200-430	27	24.7	44.5	855	195
Vitamin B3 Niacin (mg)	1.1-5.7	0.2	0.1	0.2	7.4	1.3
Vitamin B5 Pantothenate (mg)	0.6-2.2	0.2	0.3	0.5	0.5	0.5
Vitamin B6 Pyridoxine (µg)	70-290	6.2	4.3	7.7	119	108
Vitamin B12 Cobalamin (µg)	0.1-0.6	0	0	0	0	0.4
Biotin (µg)	3.5-15	0.5	0.4	0.7	0.7	2.1
Folic acid (µg)	23-100	5.2	7.5	13.5	13.5	94
Vitamin C (Ascorbic acid, mg)	17-43	4.4	3.1	5.6	48	13
Vitamin A (IU)	1333-3300	48	80	144	2500	976
Vitamin D (IU)	400-700 (<1000)	8	8	14.4	418	214
Vitamin E (IU)	2.2-11	0.4	0.5	0.9	0.9	5
Vitamin K (µg)	4.4-28	0.3	0.2	0.4	0.4	0.4

	Below		Above