# Humavant – Human Milk Fortifier
## Royal Hospital for Women Newborn use only

**2023**

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| **Alert** | Food for Special Medical Purpose as per Food Standards Australia New Zealand (FSANZ) Imported from USA and registered in New South Wales.<br>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 H2MF<br>Humavant+8 H2MF<br>Humavant Cream CR |
| **Presentation** | **Humavant+6 H$^2$MF -** 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).<br><br>**Humavant+8 H$^2$MF** - 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).<br><br>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$^2$MF (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$^2$MF | 80-120mL/kg/day | 27kcal/30mL (90kcal/100ml) |
| Humavant+8 H$^2$MF | 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 |

<table>
<tr><td></td><td>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.</td></tr>
<tr><td>Route</td><td>Intragastric tube feedings</td></tr>
<tr><td>Preparation</td><td>1. Select correct humavant preparation based on feeding order.<br>2. Thaw Humavant fortifier in Calesca milk warmer.<br>3. Using aseptic technique, add EHM/PDHM to thawed fortifier as indicated below:<br><br>a. Humavant+6 H²MF<br>i. 50ml preparation: Add 35mL of EBM/PDHM to 15mL of thawed bottle of fortifier to make a 27kcal/30mL solution (90kcal/100mL).<br>ii. 100ml preparation: Add 70mL of EBM/PDHM to 30ml of thawed bottle of fortifier to make a 27kcal/30mL solution (90kcal/100mL).<br>b. Humavant+8 H²MF<br>Add 60mL of EHM/PDHM to 40mL of thawed bottle of fortifier to make a 29kcal/30mL solution (95kcal/100mL).<br><br>c. Humavant Cream CR<br>Add thawed Cream CR to EHM/PDHM + Humavant mixture (as prescribed by NICU team/dietitian as per below recipes)<br><br>
<table>
<tr><th>Feed order</th><th>Humavant (mL)</th><th>EBM / PDHM (mL)</th><th>Cream CR (mL)</th><th>Kcal/kg/day increase</th></tr>
<tr><td>EBM/PDHM + Humavant +6</td><td>15</td><td>35</td><td>0</td><td></td></tr>
<tr><td>+ Cream CR 2kcal/30mL</td><td>15</td><td>35</td><td>2</td><td>10</td></tr>
<tr><td>+ Cream CR 4kcal/30mL</td><td>15</td><td>35</td><td>4</td><td>20</td></tr>
<tr><td>EBM/PDHM + Humavant +6</td><td>30</td><td>70</td><td>0</td><td></td></tr>
<tr><td>+ Cream CR 2kcal/30mL</td><td>30</td><td>70</td><td>4</td><td>10</td></tr>
<tr><td>+ Cream CR 4kcal/30mL</td><td>30</td><td>70</td><td>8</td><td>20</td></tr>
<tr><td>EBM/PDHM + Humavant +8</td><td>40</td><td>60</td><td>0</td><td></td></tr>
<tr><td>+ Cream CR 2kcal/30mL</td><td>40</td><td>60</td><td>4</td><td>10</td></tr>
<tr><td>+ Cream CR 4kcal/30mL</td><td>40</td><td>60</td><td>8</td><td>19</td></tr>
</table>
4. Gently swirl bottle to mix; DO NOT SHAKE.<br>5. Measure out the fortified milk using sterile syringes according to the feeding order.<br>6. Label each syringe with EBM/PDHM and patient identifier label and refrigerate (2°C to 8°C) until administered.<br>7. Administer within 24 hours from the beginning of thawing process.</td></tr>
<tr><td>Administration</td><td>Warm fortified human milk in milk warmer and administer via intragastric tube</td></tr>
<tr><td>Monitoring</td><td>Watch for feeding intolerance</td></tr>
<tr><td>Contraindications</td><td>Any condition in which enteral feeding is contraindicated.</td></tr>
<tr><td>Precautions</td><td>None</td></tr>
<tr><td>Adverse Reactions</td><td>Increased gastric residuals, abdominal distension, vomiting.</td></tr>
<tr><td>Compatibility</td><td>Not applicable.</td></tr>
<tr><td>Incompatibility</td><td>Not applicable.</td></tr>
<tr><td>Stability</td><td>2-year shelf life for frozen product.<br>Administer within 24 hours from the beginning of thawing process.</td></tr>
<tr><td>Storage</td><td>Store at -20°C<br>Do not refreeze.<br>Keep thawed product refrigerated until used at 2°C to 8°C (for no more than 24 hours, then discard)</td></tr>
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| **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]<br><br>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).<br><br>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. |
| **References** | 1. Embleton ND, Moltu SJ, Lapillonne A, van den Akker CH, Carnielli V, Fusch C, Gerasimidis K, van Goudoever JB, Haiden N, Iacobelli S, Johnson MJ. Enteral nutrition in preterm infants (2022): a position paper from the ESPGHAN committee on nutrition and invited experts. Journal of Pediatric Gastroenterology and Nutrition. 2022 Oct 21:10-97.<br>2. Grace E, Hilditch C, Gomersall J, Collins CT, Rumbold A, Keir AK. Safety and efficacy of human milk-based fortifier in enterally fed preterm and/or low birthweight infants: a systematic review and meta-analysis. Archives of Disease in Childhood-Fetal and Neonatal Edition. 2021;106(2):137-42.<br>3. Sullivan S, Schanler RJ, Kim JH, et al. An exclusively human milk-based diet is associated with a lower rate of necrotizing enterocolitis than a diet of human milk and bovine milk-based products. J Pediatr 2010;156:562–7.<br>4. O'Connor DL, Kiss A, Tomlinson C, et al. Nutrient enrichment of human milk with human and bovine milk-based fortifiers for infants born weighing <1250 g: a randomized clinical trial. Am J Clin Nutr 2018;108:108–16.<br>5. Assad M, Elliott MJ, and Abraham JH. Decreased cost and improved feeding tolerance in VLBW infants fed a human milk diet. Journal of Perinatology (2015), 1-5. doi:10.1038/jp.2015.168.<br>6. Hair AB, Bergner EM, Lee ML et al. Premature Infants 750–1,250 g Birth Weight Supplemented with a Novel Human Milk-Derived Cream Are Discharged Sooner. Breastfeeding Medicine 2015;11(3):131-137.<br>7. Cristofalo EA, Schanler RJ, Blanco CL, et al. Randomized Trial of Exclusive Human Milk versus Preterm Formula Diets in Extremely Premature Infants. The Journal of Pediatrics 2013;163(6):1592–1595.<br>8. Ghandehari H, Lee ML, Rechtman DJ et al. An exclusive human milk-based diet in extremely premature infants reduces probability of remaining on total parenteral nutrition: a reanalysis of the data. BMC Research Notes 2012, 5:188.<br>9. Hair Am, Hawthorne KM, Chetta KE et al. Human milk feeding supports adequate growth in infants <= 1250 grams birth weight. BMC Research Notes 2013; 6:459.<br>10. Hair AB, Blanco CL, Moreira AG et al. Randomized trial of human milk cream as supplement to standard fortification of an exclusive human milk-based diet in infants 750 to 1250 g birth weight. J Pediatr 2014;165(5):915-20.<br>11. Abrams SA, Schanler RJ, Lee ML, et al. Greater mortality and morbidity in extremely preterm infants fed a diet containing cow milk protein products. Breastfeeding Medicine 2014;9(6):281-285.<br>12. Hair AB, Peluso AM, Hawthorne KM et al. Beyond Necrotizing Enterocolitis Prevention: Improving Outcomes with an Exclusive Human Milk–Based Diet. Breastfeeding Med 2016;11(2).<br>13. Ganapathy V, Hay J, Wand Kim JH. Costs of necrotizing enterocolitis and cost-effectiveness of exclusively human milk-based products in feeding extremely premature babies. Breastfeeding Med 2012;7(1): 29-37.<br>14. Koletzko B, Poindexter B, Uauy R. Nutritional care of preterm infants. Scientific basis and practical guidelines. World Rev Nutr Diet 2016; Vol 110. Appendix 2. Pages 304-5. |

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| | 15. Boyce C, Watson M, Lazidis G, Reeve S, Dods K, Simmer K, McLeod G. Preterm human milk composition: a systematic literature review. British Journal of Nutrition 2016;116(6):1033-45.<br>16. Gidrewicz DA, Fenton TR. A systematic review and meta-analysis of the nutrient content of preterm and term breast milk. BMC pediatrics 2014; 14:1-4. |


| VERSION/NUMBER | DATE |
|---|---|
| **Original 1.0** | **22/12/2023** |
| **REVIEW** | 22/12/2028 |

**Authors contribution**

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|---|---|
| Original author/s | Srinivas Bolisetty, Eszter Jozsa, Sarah Allworth, Ruth Jackson, Maddie O'Connor, Anna Scott-Murphy |

| Nutrients | ESPGHAN 2022[1] Consensus | Preterm Human milk per 100 mL[14,15]* | Humavant+6 H²MF | | Humavant+8 H2MF | |
|---|---|---|---|---|---|---|
| | | | per 100mL | at 180mL/kg | per 100 mL | at 180mL/kg |
| Osmolality mOsm/kg | | | 374 | 374 | 382 | 382 |
| Volume, mL | 135-180 | 100 | 100 | 180 | 100 | 180 |
| Energy, kcal/100mL | 115-140 (-160) | 67.0 (20kcal/30ml) | 90.6 (27kcal/30ml) | 163 kcal/kg | 97.9 (29kcal/30ml) | |
| Protein, g | 3.5-4.0 (-4.5) | 1.1 | 2.0 | 3.6 | 2.3 | 4.1 |
| Fat, g | 4.0-8.1 | 3.5 | 5.4 | 9.7 | 5.9 | 10.6 |
| Linoleic acid, mg | 385-1540 | 480 | - | - | - | - |
| α-linolenic acid, mg | ≥55 | 30 | - | - | - | - |
| Docosahexaenoic acid (DHA), mg | 30-65 | 11.2 | - | - | - | - |
| Arachidonic acid, mg | 30-100 | 16.5 | - | - | - | - |
| Eicosapentaenoic acid, mg | <20 | | - | - | - | - |
| Carbohydrate, g | 11-15 (-17) | 6.7 | 7.2 | 13.0 | 7.2 | 13.0 |
| Na, mmol | 3.0-5.0 | 1.2 | 2.9 | 5.2 | 3.1 | 5.6 |
| Cl, mmol | 3.0-5.0 | 1.6 | 2.9 | 5.2 | 3.0 | 5.4 |
| K, mmol | 2.3-4.6 | 1.3 | 2.4 | 4.3 | 2.4 | 4.3 |
| Ca, mmol | 3.0-5.0 | 0.6 | 3.1 | 5.6 | 3.1 | 5.6 |
| P, mmol | 2.2-3.7 | 0.5 | 2.2 | 4.0 | 2.2 | 4.0 |
| Mg, mmol | 0.4-0.5 | 0.14 | 0.37 | 0.66 | 0.36 | 0.65 |
| Iron, mg | 2.0-3.0 (-6.0) | 0.1 | 0.1 | 0.18 | 0.1 | 0.18 |
| Zn, mg | 2.0-3.0 | 0.4 | 1.5 | 2.7 | 1.5 | 2.7 |
| Cu, µg | 120-230 | 38 | 116 | 209 | 115 | 207 |
| Selenium, µg | 7-10 | 2.4 | 4.5 | 8.1 | 5.2 | 9.4 |

| | | | | | | |
|---|---|---|---|---|---|---|
| Manganese, µg | 1-15 | 0.4 | 5.8 | 10.4 | 5.9 | 10.6 |
| Iodine, µg | 11-55 | 17.8 | 20 | 36 | 21 | 38 |
| Taurine, mg | | 4 | - | - | - | - |
| Carnitine, mg | | 0.7 | - | - | - | - |
| Chromium, µg | 0.03-2.25 | | - | - | - | - |
| Molybdenum, µg | 0.3-5.0 | | - | - | - | - |
| Thiamine (B1), µg | 140-290 | 8.9 | 8 | 14 | 8 | 14 |
| Pantothenic acid, mg | 0.6-2.2 | 0.2 | 0.2 | 0.4 | 0.2 | 0.4 |
| Biotin, µg | 3.5-15 | 0.5 | 0.4 | 0.7 | 0.3 | 0.5 |
| Niacin, µg | 1100-5700 | 0.2 | 0.1 | 0.2 | 0.1 | 0.2 |
| Ascorbic acid, mg | 17-43 | 4.4 | 3.1 | 5.6 | 2.6 | |
| Riboflavin (B1), µg | 200-430 | 27 | 24.7 | 44.5 | 24.8 | 44.5 |
| Pyridoxine (B6), µg | 70-290 | 6.2 | 4.3 | 7.7 | 3.7 | 6.7 |
| Folic acid, µg | 23-100 | 3.1 | 6.1 | 11.0 | 7.1 | 12.8 |
| Cobalamin (B12), µg | 0.1-0.6 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| Vitamin A, IU<br>(µg retinol ester) | 1333-3300<br>(400-1000) | 48<br>(14.4) | 79.7<br>(24.0) | 143.5 | 99.7<br>(29.9) | 179.5 |
| Vitamin D, IU (<1000) | 400-700 | 8.0 | 8.0 | 14.4 | 8.0 | 14.4 |
| Vitamin E, IU | 2.2-11 | 0.4 | 0.5 | 0.9 | 0.4 | 0.7 |
| Vitamin K, µg | 4.4-28 | 0.3 | 0.2 | 0.4 | 0.2 | 0.4 |

1 mmol Na=23 mg: 1mmol Cl = 35.5 mg; 1 mmol K= 39.1 mg; 1 mmol Ca=40 mg; 1 mmol P = 31 mg; 1 mmol Mg = 24.3 mg. 1:1 Ca:Ph molar ratio is equal to 1.3: 1 weight(mg) ratio.

*Preterm human milk values: Protein and carbohydrate content values are adapted from Boyce et al.[15] Remaining values are adapted from Nutritional Care of Preterm Infants: Scientific Basis and Practical Guidelines.[14]