# Neonatal Parenteral Nutrition (TPN) – Full Neonatal Clinical Guideline – Joint Derby and Burton

Reference no.:CG-NICU/3181/22

**Table of contents:**

Significant changes from previous guideline:

- Change to presentation options for full PN to use off-the-shelf products, or bespoke outsourcing where there are individualised requirements; associated minor changes to content of PN regimens:
    - Approx 8% increase in glucose content of standard preterm regimen for central administration
    - Approx 10% reduction in nitrogen content when outsourcing
    - Amino acid source Primene® in place of Vaminolact® for standard preterm regimen for central administration/outsourced bespoke option
- Modifications to lipid details (section 1.5, protection from light; section 1.6 table, presentation options for PN; and Lipid section of appendix I)
- Process for QHB NNU removed as no longer required

## 1.1 Purpose

To support neonatal care providers in ensuring that premature and low birth weight infants receive optimal nutrition when they are unable to meet their requirements by enteral feeding alone. This guideline refers to practice at both the Derby site and Burton site of UHDB.

## 1.2 Glossary of terms:

| | |
|---|---|
| **CASU** | RDH Pharmacy Central Aseptic Services Unit |
| **GA** | Gestational Age |
| **NBM** | Nil by mouth |
| **PN** | Parenteral Nutrition |
| **TPN** | Total Parenteral Nutrition |
| **UHDB** | University Hospitals of Derby and Burton NHS Foundation Trust |
| **UVC** | Umbilical Venous Catheter |
| **LL** | Long Line |

## 1.3 Indications for Parenteral Nutrition (PN)

PN should be considered for any premature or low birth weight infant, either as a nutritional supplement or total parenteral nutrition for infants who are nil by mouth (NBM) or receiving trophic feeds. If the preterm infant fits the criteria below, PN should be started as soon as possible, within at least 8 hours.

Particular indications include:

- Prematurity: GA <31/40
- Prematurity: GA ≥31/40 where sufficient progress is not made with enteral feeding in the first 72 hours after birth
- Intrauterine growth restriction (IUGR) with absent or reversed end diastolic flow (AREDF)
- NBM due to *e.g.* suspected necrotising enterocolitis (NEC)
- Infants not tolerating enteral feeds or enteral feeds stopped for ≥48 hours

**Exclusions for Pre-term Parenteral Nutrition**

Infants >28 days after birth.

This guideline covers babies born preterm, up to 28 days after their birth date and babies born at term up to 28 days after their birth.

## 1.4 Access and Administration of Neonatal PN

The preterm standard PN must be administered via a central line (umbilical venous catheter [UVC] or long line [LL]) due to the high concentration of glucose (15%) and resulting high osmolality. If central access is not possible peripheral PN may be administered via a peripheral cannula. This is less ideal because the nutritional content is reduced (amino acids reduced by ~40%, glucose reduced by ~30%, total energy reduced by ~25%). It is ordered as required from an external manufacturer.

Peripheral nutrition should only be considered if:

1. It would avoid a delay in commencing PN
2. Short term use of peripheral venous access is anticipated i.e. < 5 days
3. Central access is unsuitable or not desirable *e.g.* suspected line sepsis

The aqueous bag can be infused for up to 48 hours if run through a 0.22-micron filter; the lipid component must be used with a filter size of no less than 1.2 microns to allow lipid molecules to pass through. The lipid must be changed every 24 hours.

On administration of PN a 3-phase independent check should be done by 2 nurses:

1. Confirm prescription against bag
2. Confirm correct patient and weight
3. Confirm correct rate(s) and infusion channel for each component (including pump line label used)

There is space to document these checks at the bottom of the prescription.

## 1.5 Protection from light

In September 2019 an alert was issued jointly by the MHRA and EMA regarding the importance of protecting PN from light prior to and during administration. This is due to the potential formation of peroxides and other degradation products in measurable quantities when amino acid or lipid solutions containing vitamins are exposed to natural or environmental light, particularly phototherapy. A meta-analysis has demonstrated that light protection reduces mortality at 36 weeks[i]. Light protection in this case refers to light-proof covers over PN infusion bags during storage and administration, as well as light-protected lines.

Both the aqueous and lipid parenteral nutrition solutions should therefore be protected from light whilst being stored and whilst being infused to protect against oxidation of the amino acids, trace elements and vitamins it contains. PN should be administered using light-protective giving sets, light-protective lines and light-protective bags; white or silver for the aqueous bag and brown or black for the lipid component unless the lipid is supplied in amber-tinted 50mL UV-protect syringes (see section 1.6, Presentation of PN).

Where possible, white ITH Pharma bag covers will be used to protect the aqueous PN.

*If Numeta is used as 3-chamber bag (3CB) then this must be changed daily and not administered through a filter. If Numeta is used as 2-chamber PN (i.e. glucose, amino acids and electrolytes only) then this can be infused through a filter over 48 hours, but a separate lipid bag will be needed, and this must be changed daily and not filtered.*

## 1.6 Presentation of PN

Early PN is delivered as an aqueous infusion only at UHDB. Full PN is presented in two phases, described as the 'aqueous phase' and the 'lipid phase' which run concurrently. See 1.9 for description of early vs full regimens. Presentation options are shown in the table below.

<table>
<tr><th colspan="5">Presentation options</th></tr>
<tr><td>Early ('starter') PN</td><td>Aqueous phase (only)</td><td colspan="3">A<br>Stocked starter infusion bag for central administration; includes nitrogen, glucose, electrolytes at set levels (see appendix I)<br><br>'Royal Derby Preterm Starter 160ml'<br><br>Formulation ITH00000395<br><br>Stocked on NICU; replenished from pharmacy CASU</td></tr>
<tr><td rowspan="3">Full PN</td><td rowspan="2">Aqueous phase<br><br>Glucose, amino acids, electrolytes, trace elements</td><td rowspan="2">B<br>Stocked preterm infusion bag for central administration (standard regimen); includes nitrogen, glucose, electrolytes and trace elements at set levels (see appendix I)<br><br>'Royal Derby Preterm 610ml with Peditrace (2024)'<br><br>Formulation ITH00001234<br><br>Stocked and dispensed from pharmacy CASU</td><td>C<br>Outsourced peripheral regimen; includes nitrogen, glucose & electrolytes at lower set levels than B (see appendix I)</td><td>D<br>Bespoke outsourced infusion bag including nitrogen, glucose, electrolytes and trace elements - to mimic baseline content of B (for central administration), but with tailored electrolyte content (within stability limits)</td></tr>
<tr><td colspan="2">(C & D) Outsourced to ITH Pharma by pharmacy CASU<br><br>Deadline for prescription receipt in pharmacy 10am for same-day delivery (11am for next day delivery)</td></tr>
<tr><td>Lipid phase<br><br>Lipid plus water- and fat-soluble vitamins</td><td colspan="2">E<br>Amber-tinted 50ml syringe, containing bespoke volume Intralipid® & vitamins plus overage<br><br>Prepared in-house</td><td>F<br>Off-the shelf infusion bag containing lipid and vitamins (when available)<br><br>Fresenius Kabi compounded PN 'SMOFlipid® with vitamins'<br><br>JPN91268001</td></tr>
</table>

## 1.7 Considerations for PN

Enteral feeding is required for maturation of the normal functioning of the gastrointestinal tract, so where possible enteral feeds should be encouraged as tolerated. PN should be considered supportive in this regard, rather than a replacement for enteral feeding.

PN is available as a standardised, pre-made bag (see appendix I for nutritional content) with maintenance electrolytes included. An infant with high serum levels of sodium (if not thought to be dehydration) or potassium (if not a result of a partially haemolysed blood sample) may require a reduction in PN rate to reduce the provision of electrolytes already in excess. The same applies to calcium and phosphate, but a senior clinician's advice should be sought as to whether the serum levels justify a reduction in nutrition provision. This decision will likely include an assessment of the infant's nutritional deficit (based on gestational age and birth weight) and predicted duration of suboptimal enteral feeding. It is worth noting that (with the exception of phosphates) electrolytes are exclusively contained within the aqueous (amino acid / glucose) bag, so lipid rate need not be reduced.
Due to low usage (and resultant wastage of stock), the term PN regimen is no longer provided. In certain circumstances it may be possible to use preterm PN for a term infant (see information in appendix 1), but it is important to consider that preterm PN is designed to meet the higher nutritional requirements of a preterm infant, so a rate reduction may be necessary. Please discuss further with a pharmacist. PN is usually less critical for term infants as they have had an opportunity to build up some fat reserves throughout the 3$^{rd}$ trimester.

## 1.8 Aims of PN administration

- To optimise nutritional intake of infants who are being cared for on NICU and NNU.
- To optimise growth and development. Traditionally weight gain has been used to assess an infant's growth, but head growth is also an important consideration, as this directly correlates to brain growth and has been shown to improve neurodevelopmental outcomes.
- To provide an appropriate quantity of maintenance electrolytes, which should be adjusted to the infant's requirements, based on serum levels and clinical condition.
- To monitor the infant for signs that PN is not being tolerated *e.g.* hepatic dysfunction (typically after prolonged TPN).

## 1.9 Neonatal PN Regimens

There are three types of PN available for use:

1. Starter (for central administration) (Early PN)
2. Preterm (for central administration) (Full PN)
3. Peripheral (Full PN)

The composition of these types is pre-defined; additional electrolytes are possible with the Preterm bags for central administration, on an **outsourced** basis only.

**Stages of parenteral nutrition**

**Early/Starter PN** – This stage of PN is intended to be started as soon as possible after the infant's birth, usually within a few hours after delivery. Its primary goal is to prevent excessive catabolism by providing energy and protein. Secondary goals include prevention of hypocalcaemia. In this phase, PN contains glucose, amino acids, calcium, potassium, magnesium and phosphate; but not sodium.

**Full Preterm PN** – This stage of PN is intended to meet the entire nutritional needs of the infant and support normal rates of growth. To do so, it must contain a wide range of essential nutrients, and sufficient protein and energy to support growth.

**Energy Needs of Babies on Neonatal Parenteral Nutrition**
For preterm and term babies who need total neonatal parenteral nutrition deliver energy as follows:

If **<4 days** after birth:
- Give a starting range of 40 to 60 kcal/kg/day
- Gradually increase to a maintenance range of 75 to 120 kcal/kg/day

If **>4 days** after birth:
- Give a range of 75 to 120 kcal/kg/day

The amount of energy that is provided by concurrent enteral feeds must be deducted from the parenteral nutrition. Therefore, as the enteral feeds increase, the volume of parenteral feeds/fluids must be reduced in line with the baby's ml/kg/day requirement.

## Types of Neonatal PN available at UHDB – See Appendix 1

**Starter PN**
Starter PN is designed for use from birth until 72 hours of age. It doesn't contain sodium because infants don't begin to excrete sodium until they are 48-72 hours old. It is not intended to be infused at rates higher than 80ml/kg/day due to putting undue strain on the kidneys (80ml/kg/day of starter PN contains equivalent amino acids to 120ml/kg/day of preterm PN). Starter PN bags are kept as stock on NICU so they may be initiated at any time. Starter PN should be given via UVC or LL only.

**Preterm PN**
Preterm PN is the preferred maintenance PN regimen and is procured by pharmacy as a ready to administer product for NICU at RDH. Preterm PN should be administered centrally (UVC, LL) due to high osmolality. The PN will be supplied as two components: the aqueous bag (containing amino acids, glucose, electrolytes and trace elements) and the lipid formulation (see table in 1.6) containing lipids and vitamins. Sodium, potassium and phosphate may be added to the aqueous phase if the infant's blood results indicate that this is necessary. Where this is required, it will be outsourced; i.e., ordered on a named-patient basis from an external supplier (ITH Pharma). For same-day delivery the prescription needs to be completed by 10am (or for next day delivery, 11am).

**Peripheral PN**
Peripheral PN can be obtained for infants who require PN but have no central IV access. It is more dilute than the preterm PN regimen, which results in a lower osmolality to permit peripheral administration, but as a result it is also less nutritionally comprehensive. It should be reserved for when central IV access is deemed inappropriate *e.g.* suspected line sepsis. Where this is required, it can be ordered on a named-patient basis from an external supplier (ITH Pharma). Water-soluble vitamins can be added if no lipid PN is being infused (though note that lipid PN can be infused peripherally). For same-day delivery the prescription needs to be completed by 10am (or for next day delivery, 11am).

**Term PN**
Term PN is no longer provided at UHDB since keeping it in stock has resulted in a lot of waste due to low usage. Term babies are less nutritionally compromised at birth and have sufficient reserves (compared with a preterm or low birth weight infant) to withstand periods of suboptimal feeding. In addition, term infants in need of PN are frequently in need of surgery, which is not provided at UHDB. These infants are usually transferred to another centre within a day or two.

## 2.0 Electrolytes

**Sodium**

Note: Starter preterm PN does not contain sodium

Sodium is a permissive growth factor in infants, and since pre-term infants may also be small for gestational age (SGA) it is important to ensure that hyponatraemia is prevented and resolved promptly if it does occur.

The sodium requirement for a preterm neonate is around 3-5mmol/kg/day; the Preterm regimen provides 3.59mmol $Na^+$ per 120ml (more can be added if desired). The trend in serum sodium is at least as important as the most recent value: if serum sodium is stable at 135mmol/L, a small addition of sodium may be desirable to nudge the sodium closer to 140mmol/L; in contrast, if serum sodium has reduced from 146mmol/L to 136mmol/L in the previous 48 hours, a large addition may be necessary to prevent severe hyponatraemia. A small addition would be something in the region of a 20% increase *e.g.* from 3.5mmol/kg/day to 4mmol/kg/day. A large addition would be more like a 40% increase *e.g.* from 3.5mmol/kg/day to 5mmol/kg/day.

Sodium replenishment may be required when sodium losses are high. Note that hyponatraemia may be caused by use of excessively dilute fluid, inappropriate ADH and excessive bowel losses. Hypernatremia may be associated with excessive fluid losses, inappropriate sodium intake or renal causes. Refer to 'Electrolyte Maintenance & Replacement - Paediatric Full Clinical Neonatal Guideline' for more information.

**Potassium**

Potassium is key to nerve depolarisation, allowing signal conduction throughout the nervous system, and extremely low or high levels can result in (among other things) electrocardiographic abnormalities. The potassium requirement for a preterm infant is in the region of 2mmol/kg/day; the preterm PN provides around 2.5mmol $K^+$ per 120ml (more can be added). It is worth bearing in mind that potassium is an extracellular cation, and since neonatal bloods are usually capillary samples, most results will be haemolysed to some degree – sometimes not enough to be flagged by the pathology system as haemolysed, but it is worth considering the possibility of haemolysis, especially if they are unexpected *e.g.* suddenly raised potassium in the absence of renal impairment.

**Magnesium**

Magnesium has many important roles within the body, many of which as a component of enzymes which allow the normal functioning of everyday cellular processes. Hypomagnesaemia is also linked to hypokalaemia. Preterm PN provides around 0.2mmol $Mg^{2+}$ per 120ml (on rare occasions when this is required magnesium can be added up to a maximum allowance of 1.5mmol per 120ml).

**Calcium**

Calcium is an essential electrolyte that has wide-ranging roles in muscle contraction, nerve conduction, blood cell production, clotting and is a significant component of bone mineral. If starting PN in the first 48 hours after birth, 0.8mmol/kg/day to 1mmol/kg/day is a recommended starting dose. Increase to a maintenance range of 1.5mmol/kg/day to 2mmol/kg/day after 48 hours. When commencing PN more than 48 hours after birth, give a range of 1.5mmol/kg/day to 2mmol/kg/day. PN at UHDB provides around 2mmol $Ca^{2+}$ per 120ml and this cannot be increased further due to the risk of calcium and phosphate forming an insoluble precipitate. Where additional calcium is required, consider using 10% calcium gluconate as a separate infusion – See calcium gluconate monograph.

**Phosphate**

Persistent low hypophosphatemia can have detrimental consequences for bone health, as phosphate is required for calcium deposition. If alkaline phosphatase is elevated, this may indicate a risk of hypophosphataemia. If additional phosphate is required in the PN, this is added as sodium glycerophosphate, so for every additional 1mmol of phosphate, 2mmol of sodium will also be added. If starting parenteral nutrition in the first 48 hours after birth, 1mmol/kg/day is the advised starting dose. After 48 hours after birth, a maintenance dosage of 2mmol/kg/day is recommended. A starting dose of 2mmol/kg/day is advised in neonates starting PN 48 hours after birth. UHDB defaults to provide 1.85mmol/kg/day when run at 120mL/kg/day in the first 48 hours of receiving preterm PN (which has been found to be appropriate in practice). Give a higher dosage of phosphate if indicated to do so by serum phosphate monitoring. Be aware that preterm babies may be at risk of phosphate deficit requiring additional phosphate supplementation.

*A calcium to phosphate ratio of between 0.75:1 and 1:1 is recommended for preterm and term babies on neonatal PN. UHDB regimens default to provide this ratio without additional electrolyte supplementation.

**Chloride**

Excessive chloride can contribute to or worsen metabolic acidosis (chloride in plasma retains hydrogen ions in the blood), therefore electrolyte salts other than chloride *e.g.* sodium glycerophosphate, potassium acetate, magnesium sulphate are more popular choices. However, sodium and potassium added to the PN are usually added as the chloride salt. Sodium can be added as glycerophosphate, but for every 2mmol of sodium added, 1mmol of phosphate must also added.

**Vitamins**

A full range of water-soluble and fat-soluble vitamins are included in the lipid portion of all regimens. Details of amounts added are given in Appendix I. If no lipid is prescribed, water-soluble, but not fat-soluble, vitamins can be added to the aqueous phase.

**Trace elements**

A full range of trace elements are included from the trace element solution, Peditrace® to give a complete feed. Amounts added are given in Appendix I.

**Iron**

Iron is not present in Peditrace® and is not routinely added to neonatal PN. Where a preterm baby is on PN for more than 28 days, ferritin, iron and transferrin saturation need measuring. Do not give intravenous parenteral iron supplements to preterm or term babies on neonatal PN who are less

than 28 days. For preterm babies who are older than 28 days, and are on parenteral PN, continue to monitor for iron deficiency and treat if necessary.

## 2.2 Ordering Process for PN

Once the neonate is ready to move from Starter to Preterm PN, the ward pharmacist for NICU should use the appropriate prescription, which routinely covers a 48-hour period. Once the prescription is agreed with the neonatal registrar or consultant on the ward, the prescription requires printing and delivering to CASU at RDH.

The RDH pharmacy central aseptic unit (CASU) will supply standard PN required for babies on NICU same day as requested, so long as the PN prescription is received by 1pm.

**Where meeting individualised electrolyte requirements is necessary the PN will be supplied by an external manufacturer. The prescription needs to be received by CASU before 10am and handed to the chief technician to organise ordering.** The order is received by 6pm that day and on receipt will be checked against the prescription by the CASU team and NICU contacted to arrange collection.

Process for RDH:
Ward pharmacist to bring signed prescription to CASU and hand over to the chief technician. Once PN is ready, CASU will organise collection with NICU. As the prescription is a 48-hour prescription, the ward pharmacist will need to inform CASU whether the lipids are required on day 2 of the prescription.

Process for Weekends:
CASU do not supply PN over the weekend. Any babies requiring PN over a weekend will need a prescription submitting to cover Saturday, Sunday and Monday on a Friday.

For example, on a Friday you will need to send two prescriptions, one to cover Friday and Saturday and another to cover Sunday and Monday, allowing Monday daytime for CASU to make and supply Monday and Tuesdays PN. Any questions, contact CASU before midday on a Friday.

For any babies identified as needing PN after 1pm on a Friday, there will not be time to organise lipid PN if SMOFlipid with vitamins is not available, in which case CASU will supply standard aqueous-phase PN only. Note that from Friday evening (when CASU is not open) babies should commence starter PN as this can reasonably be used for up to 72 hours. CASU will pick up supply of full PN on Monday, if required.

Process for Bank Holidays:
As per the weekend process, CASU do not supply PN over bank holidays. Where babies require PN over the weekend leading into a bank holiday, starter PN should be commenced. After 72 hours, the MDT should decide whether the introduction of electrolytes such as sodium and potassium are required; these can supplement or be in place of the starter PN depending on results.

# 2.1 Monitoring Guidance

| Component to be measured | | Daily | Twice Weekly | Weekly | Monthly | Specifically |
|---|---|---|---|---|---|---|
| **Phosphate** *(Serum or plasma)* | Initiation | ✓ | | | | |
| | Maintenance | | | ✓ | | More frequently where there is clinical concern or a previous result outside the normal range or those born at <32$^{+0}$ weeks |
| **Iron** | | | | | ✓ | Once baby is on PN for more than 28 days |
| **Liver function tests** | | | | ✓ | | More frequently where there is clinical concern or previous deranged LFTs |
| **Serum Triglycerides** | **Initiation** | ✓ | | | | |
| | **Maintenance** | | | | | More frequent where the level is elevated or risk of hypertriglyceridemia |
| **Blood pH, potassium, chloride and calcium** | **Initiation** | ✓ | | | | More frequently where there is clinical concern or a result(s) outside the normal range, or whereby doses of IV components have been changed |
| | **Maintenance** | | | ✓ | | |
| **Blood glucose** | | ✓ | | | | Every 1-2 hours after first initiation and change of nutritional bag or more frequently with previous hyper/hypoglycaemia or clinical reasons for concern e.g. sepsis/seizures |

## Appendix I – Types of Neonatal PN available at UHDB

**Table: PN Regimens at a glance** (see also section 1.6)

| **Per 100ml PN** (inc. lipid portion where appropriate) | **Starter PN** | **Preterm PN** (with 3g/kg/day lipid[1]) | **Peripheral PN** (outsourced) (with 3g/kg/day lipid) | **Numeta G13%[2]** |
|---|---|---|---|---|
| Amino acids | 3.9g | 3.0g[3] | 1.9g | 3.1g |
| Glucose | 15g | 13.7g | 9.4g | 13.3g |
| Lipid | × | 2.5g | 2.5g | 2.5g |
| Sodium | × | 2.9mmol | 2.5mmol | 2.2mmol |
| Potassium | 1 | 2.1mmol | 2.1 mmol | 2.1mmol |
| Calcium | 1 | 1.7 mmol | 0.84 mmol | 1.3mmol |
| Magnesium | 0.2 | 0.16 mmol | 0.17 mmol | 0.16mmol |
| Phosphate | 1 | 1.7 mmol | 0.85 mmol | 1.3mmol |
| Acetate | × | 2.1 mmol | × | 2.4mmol |
| Chloride | × | 0.48 mmol | 3.4 mmol | 3.1mmol |
| Further electrolyte additions permitted | × | only by outsourcing | × | × |
| Vitamins | × | ✓in lipid phase | ✓in lipid phase | × |
| Trace elements | × | ✓ | ✓ | × |
| Stock on NICU | ✓ | × | × | × |
| Route of administration | Central | Central | Peripheral | Central |
| Aqueous bag total volume | 160ml | 610ml | 500ml | 300ml |
| Lipid component | × | ✓ (separate) | ✓(separate) | ✓(3CB) |
| Maximum rate (inc lipid portion where appropriate) | 80ml/kg/day | 120ml/kg/day | 120ml/kg/day | 127.9ml/kg/day |
| When to be used | Up to 72 hours of age | From 24 hrs of age | From 24 hrs of age | From 24 hours of age |

The starter bag can be infused for up to 48 hours and should be run through an inline 0.22-micron filter.

[1] 100ml PN when on lipids at 17.5ml/kg/day includes 85.4ml aqueous component which contains the stated nitrogen/amino acids (for Preterm and Peripheral PN; starter PN is aqueous component only)
[2] Numeta can be used as a 2-chamber bag (2CB) or a 3-chamber bag (3CB); this guideline assumes it is being used as a 3CB. See Numeta section for more info. Addition of extra electrolytes, and vitamins/trace elements, is theoretically possible but not at UHDB as there is no mechanism for doing so.
[3] The formulation stability matrix necessitates a slightly lower (~10%) nitrogen content, if outsourcing for additional electrolytes to be added. NICE guideline recommends a maintenance range of 3 to 4 g/kg/day of amino acids per day [Neonatal parenteral nutrition (NG154) 9 Feb 2020]. When on full rate preterm PN (120ml/kg/day of which 17.5ml/kg/day is lipids) the baby receives 3.6g amino acids, or, if the formulation is outsourced for tailored electrolytes, 3.3g amino acids.

**Term PN**

If PN is desired for a term infant, then pre-term PN may be used as follows:
Issue pre-term PN with aqueous component at 75% normal rate *i.e.* 77ml/kg/day
Order lipid component at 100% normal rate *i.e.* 17.5ml/kg/day
Top-up fluids to 120ml/kg with 10% glucose *i.e.* 25.5ml/kg/day
Please note that electrolytes such as sodium, potassium and magnesium are reduced compared to full rate aqueous PN and may need supplementing.
Aqueous PN rate can be reduced to 50% normal rate *i.e.* 51ml/kg/day.

The table before refers to the nutritional values provided by the PN at RDH site.

| Nutrition | | Preterm (full rate) | Preterm (75% aqueous rate) |
|---|---|---|---|
| Volume | ml/kg/day | 120 | 94.5 |
| Protein | g/kg/day | 3.5 | 2.5 |
| Glucose | g/kg/day | 16.4 | 13.6[4] |
| Lipid | g/kg/day | 3 | 3[5] |
| Energy | kcal/kg/day | 104 | 95.7 |
| Sodium | mmol/kg/day | 3.5 | 2.6 |
| Potassium | mmol/kg/day | 2.5 | 1.9 |
| Calcium | mmol/kg/day | 2 | 1.5 |
| Magnesium | mmol/kg/day | 0.2 | 0.15 |
| Phosphate | mmol/kg/day | 2 | 1.5 |

The maximum rate for preterm PN and peripheral PN is 120ml/kg/day – if additional intravenous fluids are required this should be provided as 5% glucose (10% glucose may be used if blood glucose is low). Where trophic enteral feeds start the increase, deductions from parenteral fluids should be taken from the glucose 5% before reducing the volume of PN.

**Numeta G13%**

| | Numeta (3CB)[6] | Preterm Regimen |
|---|---|---|
| Volume (mL/kg/d) | 127.9 | 120 |
| Protein (g/kg/d) | 4.0 | 3.5 |
| Glucose (g/kg/d) | 17.1 | 15 |
| Fat(g/kg/d) | 3.2 | 3 |
| Energy (kcal) | 116 | 104 |
| $Na^+$ (mmol/kg/d) | 2.8 | 3.5 |
| $K^+$ (mmol/kg/d) | 2.6 | 2.5 |
| $Ca^{2+}$(mmol/kg/d) | 1.6 | 2 |
| $Mg^{2+}$ (mmol/kg/d) | 0.2 | 0.2 |
| $PO_4^{3-}$ (mmol/kg/d) | 1.6 | 2.3 |

Numeta is a licensed neonatal PN product. It is not routinely used at Derby but is included in this guideline as an alternative PN if Preterm PN ever ceases to be available from ITH. Numeta is presented as a three-chamber bag, which is rolled (by production staff in CASU) to combine the chambers resulting in a single 300ml bag containing all components of the PN. Since the lipid is combined with the aqueous elements of the PN, this should not be run through an inline filter finer than 1.2microns, and the infusion should be changed daily as a consequence. It can also be used as a chamber bag, in which case the aqueous portion can be infused for up to 48 hours through a 1.2micron inline filter, but unless the infant weighs less than 0.939kg there will be insufficient volume in the bag to last 48 hours. If using as a 2-chamber bag then lipids would need to be ordered separately.

[4] Including glucose from 10% glucose infused separately to top up fluids
[5] As lipids are run at full rate
[6] Values in this table assume PN is being infused at the maximum rate *i.e.* 127.9ml/kg/day for Numeta 3CB and 120ml/kg/day for Preterm Regimen. Reduce nutritional content accordingly if fluid allowance is less.

Used as a 3CB Numeta has sufficient volume for 24 hours of PN for infants weighing up to 2.346kg. Above this weight consideration should be given to capping PN at 300ml/day with top up of 5% or 10% glucose. Electrolytes and vitamins/trace elements can be added to Numeta as dictated by the infant's blood results and clinical situation. The main differences between Preterm regimen and Numeta are highlighted in the accompanying table. It is worth noting that the concentration of glucose in Numeta is higher than in preterm PN, meaning the risk of thrombophlebitis is higher (although shouldn't be an issue if the long line is well-sited). These differences are consistent with the commonly reported adverse effects of hypophosphataemia and hyponatraemia with Numeta.

**Nutritional components of PN regimens**

**Amino acids**

Starter PN and Peripheral Preterm PN amino acids are provided by Vaminolact®, whereas Preterm PN (for central administration) amino acids are provided by Primene®. The basis for this difference is historical and motivated by stability information available. The composition of these two amino acid solutions is as follows:

| | **Vaminolact** | **Primene** |
|---|---|---|
| **Amino acid** | **Content per 100ml** | |
| Glutamic acid | 710mg | 1000mg |
| Leucine | 700mg | 1000mg |
| Alanine | 630mg | 800mg |
| Lysine | 560mg | 1100mg |
| Proline | 560mg | 300mg |
| Arginine | 410mg | 840mg |
| Aspartic acid | 410mg | 600mg |
| Serine | 380mg | 400mg |
| Threonine | 360mg | 370mg |
| Valine | 360mg | 760mg |
| Isoleucine | 310mg | 670mg |
| Phenylalanine | 270mg | 420mg |
| Glycine | 210mg | 400mg |
| Histidine | 210mg | 380mg |
| Tryptophan | 140mg | 200mg |
| Methionine | 130mg | 240mg |
| Cysteine | 100mg | 189mg |
| Tyrosine | 50mg | 45mg |
| Taurine | 30mg | 60mg |
| Ornithine HCl | 0 | 318mg |

**Composition of Vitamin and Trace Mineral Additives**

**<u>Water soluble vitamins – Solivito N</u>**

1/10th standard vial per kg is added to the lipid providing:

| | |
|---|---|
| Thiamin ($B_1$) | 0.32 mg/kg/day |
| Riboflavin ($B_2$) | 0.36 mg/kg/day |
| Nicotinic acid | 4 mg/kg/day |

| | |
|---|---|
| Vitamin $B_6$ | 0.4 mg/kg/day |
| Pantothenic acid | 1.5 mg/kg/day |
| Biotin | 6 microgram/kg/day |
| Folic acid | 0.04 mg/kg/day |
| Vitamin $B_{12}$ | 0.5 micrograms/kg/day |
| Vitamin C | 10 mg/kg/day |

**Fat soluble vitamins – Vitlipid N Infant®**

Infants ≤ 2.5 kg will receive 4 ml/kg Vitlipid N Infant®, included in the lipid phase of the PN regimen, providing per kg per day:

| | |
|---|---|
| Vitamin A | 276 micrograms (920 units)/kg/day |
| Vitamin D | 4.0 micrograms (160 units)/kg/day |
| Vitamin E | 2.56 mg (2.8 units)/kg/day |
| Vitamin K | 80 micrograms/kg/day |

Infants >2.5 kg cannot be given SMOFlipid with vitamins at the standard rate of lipid administration on the Preterm regimen as they will receive more than the maximum dose of 10 ml Vitlipid N daily, therefore a bespoke lipid product would need to be outsourced or the total volume of SMOFlipid with vitamins administered capped at 45ml per day. It is unlikely that a baby of this weight would receive PN at RDH.

**Trace Minerals**

**Peditrace®** 1ml/kg/day added to aqueous bag provides:

| | |
|---|---|
| Zinc | 3.82 micromoles/kg/day |
| Manganese | 18.2 nanomoles/kg/day |
| Selenium | 2.3 nanomoles/kg/day |
| Fluoride | 3 micromoles/kg/day |
| Iodine | 7.88 nanomoles/kg/day |
| Chloride | 20 micromoles/kg/day |

The stocked preterm infusion bag (ready to administer centrally) - 'Royal Derby Preterm 610ml with Peditrace (2024)' Formulation ITH00001234 contains Peditrace to deliver 1ml/kg plus or minus 2% when babies are receiving PN at the 2g/lipid/day or 3g/lipid/day rate respectively.

**Energy**

Non-nitrogen energy is provided by glucose alone in the Starter Preterm regimen and glucose and fat (lipid) in an energy ratio of approximately 2.4:1 in Preterm regimens[7]. The goal is to promote good nitrogen retention. The Peripheral regimen has a lower ratio of glucose to fat due to the detrimental effect of glucose and beneficial effect of lipid on the patency of peripheral veins but provides less complete nutrition overall.

[7] NICE committee agreed by informal consensus that a range of 60 to 75% carbohydrate to 25 to 40% lipid should be used [i.e. between 1.5:1 and 3:1]: Neonatal parenteral nutrition [D8] Ratio of carbohydrates to lipids NICE guideline NG154. Evidence reviews, February 2020.

**Glucose**
Starter PN and the aqueous bag of Preterm PN both contain greater than 12.5% glucose and should therefore be administered centrally to avoid thrombophlebitis. The aqueous bag of Peripheral PN contains 11% glucose, permitting it to be administered through a peripheral cannula. When assessing glucose intake, the percentage of glucose refers to just the aqueous portion of PN.

**Lipid**
The lipid provided is Intralipid 20% or SMOFlipid 20%. Intralipid is a purified soya bean oil emulsion, providing essential fatty acids, whereas SMOFlipid is a mixture containing, additionally, medium-chain triglycerides, refined olive oil and fish oil rich in omega-3-fatty acids. These lipids provide energy, essential fatty acids and a small quantity of organic phosphate - 15mmol/L[ii], equivalent to 0.225mmol per 3g lipid.

After infusion, the triglyceride portion is hydrolysed to free fatty acids. If the rate of infusion exceeds the rate of hydrolysis, triglyceride levels will rise. If the rate of hydrolysis exceeds the rate of free fatty acid oxidation, plasma free fatty acids will rise. These displace bound bilirubin from albumin, which may be of some concern in infants with unconjugated hyperbilirubinaemia, though the concentration of free fatty acids likely to be a problem at any concentration of albumin is unknown. Infusing lipids over 24 hours should improve lipid tolerance as the infusion rate is less likely to exceed the rate of hydrolysis. The maximum amount of fat tolerated by preterm infants is difficult to determine. U.K. neonatal units set maximum amounts of fat infused at between 2-4g fat/kg/day depending on factors such as prematurity, birth weight and whether recipients are small for gestational age as all these factors are thought to affect tolerance due to lower levels of lipoprotein lipase[iii]. Levels up to 3g/kg/day have been shown to be tolerated when infused over 24 hours[iv,v,vi], though infants born weighing <1kg are less likely to tolerate even 3g/kg/day[vii]. As the benefits of routine monitoring of triglycerides are not established, this is not undertaken.
Since optimal nutrition in the first weeks of life is important, lipids should not routinely be withheld unless there is clear evidence that lipids would be harmful *e.g.* extreme jaundice or hepatic dysfunction. Therefore, the default lipid rate for preterm PN is 3g/kg/day. In some circumstances it may be prudent to commence lipids at the lower rate of 2g/kg/day, for example if the infant is significantly jaundiced *i.e.* has bilirubin levels approaching the threshold for exchange transfusion. Infants weighing less than 1kg at birth are less likely to tolerate intravenous lipids. The lipid rate can be subsequently increased to 3g/kg/day after 48 hours if there is no evidence of intolerance.

## Appendix II – RDH Starter Preterm PN Prescription (QHB prescribe on EPMA)

**Neonatal Starter Preterm Regimen Parenteral Nutrition Prescription and Administration Record**

*Affix Patient Hospital Sticker Here*

Patient name:

Date of Birth:

Address:

Dosing weight: _____

PRESCRIPTION BASED ON:

| Major Nutrients: | | Per 60ml/kg | Per 80ml/kg |
|---|---|---|---|
| Protein | g/kg | 2.1 | 2.8 |
| Glucose | g/kg | 9 | 12 |
| Fat | g/kg | 0 | 0 |
| Sodium | mmol/kg | 0 | 0 |
| Potassium | mmol/kg | 0.6 | 0.8 |
| Calcium | mmol/kg | 0.6 | 0.8 |
| Phosphate | mmol/kg | 0.6 | 0.8 |
| Magnesium | mmol/kg | 0.12 | 0.16 |
| Total Energy | kcal/kg | 44 | 59 |

For administration via a CENTRAL LINE ONLY for up to 72 hours after birth (may be longer over bank holiday weekend)

No additions can be made to the bags.
For single use only – discard remainder
Each bag may be used for up to 48 hours
The giving set and associated lines may be used for up to 48 hours

Volume Starter Preterm PN Prescribed = _____ ml/kg/day up to a maximum 80ml/kg/day
Any extra fluid to be given as glucose 5% (or glucose 10% if blood glucose is low)

Prescriber's signature: _____ Print Name: _____

FOR NURSING STAFF USE:

| | Batch number | Expiry date | Rate set (ml/hr) | Signed by | Checked by | Time |
|---|---|---|---|---|---|---|
| Starter Preterm Bag | | | | | | |

Shaded boxes above and flow rate must be completed before administration

## Appendix III: UHDB Re-order sheet for Starter Preterm PN bag

**Neonatal Starter Preterm Regimen Parenteral Nutrition Re-order and Replacement Sheet**

COMPLETE DETAILS BELOW AND RETURN TO NEONATAL PHARMACIST DURING NORMAL WORKING HOURS FOR REPLACEMENT BAG

*Affix Patient Hospital Sticker Here*

Patient name:

Date of Birth:

Address:

Patient Gestation: _____

Dosing weight: _____

Consultant: _____

Please tick here if new bag required due to previous stock expired ☐

FOR NURSING STAFF USAGE:

| Starter Preterm bag | Batch number of bag used | Expiry date on bag used | Signed by |
|---|---|---|---|
| | | | |

PLEASE RE-SUPPLY 1 X STARTER PRETERM REGIMEN PN BAG (used for the above patient)

PHARMACY USE ONLY:

| | |
|---|---|
| Stock issued to ward by: | |
| JAC issue completed by: | |

**Appendix IV – Chart for calculation and recording of PN flow rates**

Date _____ Dosing weight 1.26 kg

Starting lipid rate 0.8 ml/hr

Starting aqueous rate 5.5 ml/hr } from prescription

Calculate any rate changes and record below

*Affix patient hospital sticker here*
Name ……
Date of birth ……
Hospital number ……
NHS number ……
Address ……
……

| Total fluid allowance (ml/day) | Total infusions other than PN (ml/day) | Enteral feeds | | Total PN rate (ml/day) | New aqueous rate (ml/hr) | New lipid rate (ml/hr) | Rate changed by | | Time rate changed |
|---|---|---|---|---|---|---|---|---|---|
| | | ml and frequency | (ml/day) | | | | | | |
| 189 | 6 | 2.5ml 2˚ | 30 | 153 | 5.5 | 0.9 | | | |
| 189 | 6 | 3ml 2˚ | 36 | 147 | 5.3 | 0.9 | | | |
| | | | | | | | | | |
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| | | | | | | | | | |
| | | | | | | | | | |

150ml/kg × 1.26kg

0.25ml/hr × 24 hrs

3ml per feed × 12 feeds per day

189ml/day – (6ml/day + 36ml/day)

= 189 – 42 = 147ml/day

0.9ml/hr × 6

147 ÷ 7 = 21ml/day lipid

÷ 24 = 0.9ml/hr

## Appendix V – PN Rate Calculations

### Neonatal PN Calculations

Below are a selection of common PN scenarios you may see on the neonatal unit. If there is a clinical need to calculate the PN rates differently to the policy, then this must be discussed with and documented by a Consultant.

**Scenario 1: Baby A weighs 1.23 kg and is having 80 ml/kg/24 hours of TPN as sole source of nutrition.**

Step One: Calculate baby's hourly fluid rate in ml/hour

e.g. 80 ml/kg/24 hours x 1.23 kg = 98.4 ml/24 hours

98.4 ml ÷ 24 hours = 4.1 ml/hour

Step Two: Split this rate between aqueous and lipid components of PN.

For the first two days that the baby receives bespoke parenteral nutrition, the lipid component accounts for ~ 10% of the volume of the total PN, so multiply the hourly rate by 0.1 - **PN prescription will state lipid PN 12.5ml/kg/day**

*E.g*. for Lipid rate: 4.1 ml/hour x 0.1 = 0.41 ml/hour (to 2 d.p)

For the first two days that the baby receives bespoke parenteral nutrition, the aqueous component accounts for ~ 90% of the volume of the total PN, so multiply the hourly rate by 0.9 - **PN prescription will state protein/glucose bag 107.5ml/kg/day**

*E.g.* for Aqueous bag rate: 4.1 ml/hour x 0.9 = 3.69 ml/hour (to 2 d.p)

In terms of rounding numbers, it is important not to round numbers until right at the end, as small changes can be amplified by your calculations.

Step Three: It is good practice to total everything after you've finished making sure the numbers make sense.

*e.g.* 0.41 ml/hour (Lipid) + 3.69 ml/hour (Aqueous) = 4.1 ml/hour

4.1 ml/hour (PN) x 24 hours = 98.4 ml/24 hours

98.4 ml/24 hours ÷ 1.23 kg = 80 ml/kg/24 hours.

**Scenario 2: Baby A weighs 1.23 kg but their fluid requirement has increased to 90 ml/kg/24 hours. They are prescribed PN, a single strength morphine infusion and they have started 1 ml/kg [to nearest 0.5 ml] of enteral feeds 2 hourly. The baby is now on their second day of bespoke parenteral nutrition.**

Step One: Calculate baby's hourly fluid rate in ml/hour

e.g. 90 ml/kg/24 hours x 1.23 kg = 110.7 ml/24 hours

110.7 ml ÷ 24 hours = 4.6 ml/hour

Step Two: Subtract feeds and infusions from hourly total.

e.g. Subtract hourly morphine rate (0.25 ml/hour) from hourly fluid requirement

4.6 ml/hour - 0.25 ml/hour = 4.35 ml/hour

Subtract hourly enteral feed amount (0.5 ml/hour) from hourly fluid requirement

4.35 ml/hour - 0.5 ml/hour = 3.85 ml/hour

Step Three: The remaining volume can now be split between aqueous and lipid components of PN.

For the first two days that the baby receives bespoke parenteral nutrition, the lipid component accounts for ~ 10% of the volume of the total PN, so multiply the hourly rate by 0.1 **PN prescription will state lipid PN 12.5ml/kg/day**

e.g. 3.85 ml/hour x 0.1 = 0.39 ml/hour (rounded to 2 d.p)

For the first two days that the baby receives bespoke parenteral nutrition, the aqueous component accounts for ~ 90% of the volume of the total PN, so multiply the hourly rate by 0.9 **PN prescription will state protein/glucose bag 107.5ml/kg/day**

e.g. 3.85 ml/hour x 0.9 = 3.47 ml/hour (rounded to 2 d.p)

In terms of rounding numbers, it is important not to round numbers until right at the end, as small changes can be amplified by your calculations.

Step Four: It is good practice to total everything after you've finished making sure the numbers make sense.

e.g. 0.25 ml/hour (Morphine) + 0.5 ml/hour (Milk) + 0.39 ml/hour (Lipid) + 3.46 ml/hour (Aqueous) = 4.6 ml/hour

4.6 ml/hour x 24 (hours) = 110.4 ml/24 hours

110.4 ml/24 hours ÷ 1.23 kg = 89.76 ml/kg/24 hours.

**Scenario 3: Baby A weighs 1.23 kg but their fluid requirement has increased to 150 ml/kg/24 hours. They are currently having 1 ml/kg [to nearest 0.5 ml] of enteral feeds 2 hourly. Their maximum PN allowance is 120 ml/kg/24 hours. Therefore, they are prescribed 5% Glucose to make up the difference in their fluid requirement.**

Step One: Calculate baby's fluid rate in ml/hour

*e.g.* 150 ml/kg/24 hours x 1.23 kg = 184.5 ml/24 hours
184.5 ml ÷ 24 hours = 7.69 ml/hour.

Step Two: Calculate the maximum PN allowance at 120 ml/kg/24 hours

*e.g.* 120 ml/kg/24 hours x 1.23 kg = 147.6 ml/24 hours
147.6 ml ÷ 24 hours = 6.15 ml/hour.

Step Three: Subtract maximum PN hourly rate (6.15 ml/hour) and hourly feed rate (0.5 ml/hour) from total requirement (7.68 ml/hour)

*e.g.* 7.69 ml/hour – 6.15 ml/hour – 0.5ml/hour = 1.04 ml/hour (to 2 d.p.) of 5% Glucose

Step Four: Work out the proportion of your Aqueous and lipid components using the PN hourly rate (6.15 ml/hour)

From day 3 of bespoke PN onwards the lipid component accounts for ~ 15% of the volume of the total PN, so multiply the new hourly rate by 0.15. **PN prescription will state lipid PN 17.5ml/kg/day**

*e.g.* 6.15 ml/hour x 0.15 = 0.92 ml/hour (rounded to 2 d.p)

From day 3 of bespoke PN onwards the aqueous component accounts for ~ 85% of the volume of the total PN, so multiply the hourly rate by 0.85. **PN prescription will state protein/glucose bag 102.5ml/kg/day**

*e.g.* 6.15 ml/hour x 0.85 = 5.23 ml/hour (rounded to 2 d.p)

In terms of rounding numbers, it is important not to round numbers until right at the end, as small changes can be amplified by your calculations.

Step Five: It is good practice to total everything after you've finished making sure the numbers make sense

*e.g.* 0.5 ml/hour (Milk) + 1 ml/hour (5% Glucose) + 0.92 ml/hour (Lipid) + 5.23 ml/hour (Aqueous) = 7.65 ml/hour
7.65 ml/hour x 24 (hours) = 183.6 ml/24 hours
182.4 ml/24 hours ÷ 1.23 kg = 149.3 ml/kg/24 hours

**Scenario 4: Baby A weighs 1.23 kg but their fluid requirement has increased to 150 ml/kg/24 hours. Their maximum PN allowance is 120 ml/kg/24 hours. They are currently having 7 ml 2 hourly of enteral feeds. To make up the difference in their fluid requirement, they are also prescribed 5% Glucose.**

Step One: Calculate how many ml/kg/24 hours are taken up by enteral feeds and other infusions

7 ml milk / 2 hours = 3.5 ml milk / hour
In 24 hours, the baby is having 3.5 ml x 24 hours = 84 ml/24 hours
84 ml/24 hours ÷ 1.23 kg = 68.29 ml/kg/24 hours (to 2 d.p)

Step Two: Subtract ml/kg/24 hours of enteral feeds and other infusions from total requirement

(From Step One) 68.29 ml/kg/24 hours is taken up by enteral feeds and other infusions
The baby's total requirement is 150 ml/kg/24 hours
150 ml/kg/24 hours – 68.29 ml/kg/24 hours = 81.71 ml/kg/24 hours remaining for PN

As 81.71 ml/kg/24 hours is less than 120 ml/kg/24 hours, we do not require any additional fluids

Step Three: Calculate baby's hourly PN rate in ml/hour

Baby requires 81.71 ml/kg/24 hours of PN
81.71 ml/kg/24 hours x 1.23 (kg) = 100.5 ml/24 hours
100.5 ml ÷ 24 hours = 4.19 ml/hour (to 2 d.p)

Step Four: Work out the proportion of your Aqueous and lipid components using the PN hourly rate (4.19 ml/hour)

From day 3 of bespoke PN onwards the lipid component accounts for ~ 15% of the volume of the total PN, so multiply the new hourly rate by 0.15. **PN prescription will state lipid PN 17.5ml/kg/day**

*e.g.* 4.19 ml/hour x 0.15 = 0.63 ml/hour (rounded to 2 d.p)

From day 3 of bespoke PN onwards the aqueous component accounts for ~ 85% of the volume of the total PN, so multiply the hourly rate by 0.85. **PN prescription will state protein/glucose bag 102.5ml/kg/day**

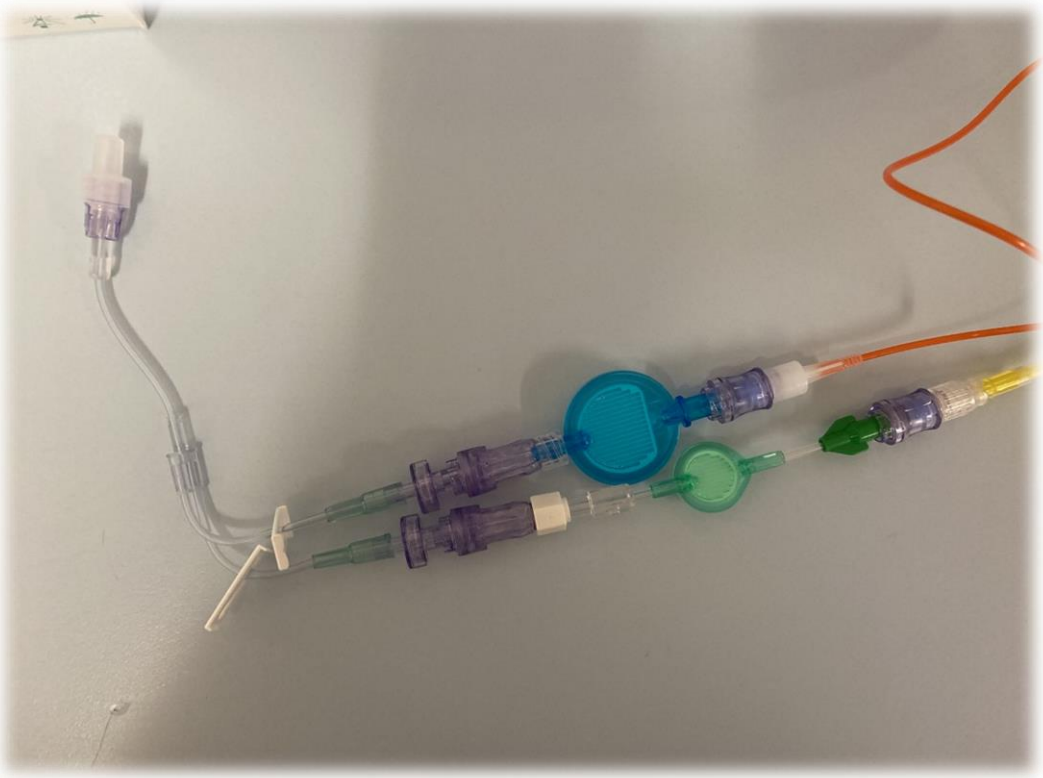
*e.g.* 4.19 ml/hour x 0.85 = 3.56 ml/hour (rounded to 2 d.p)

In terms of rounding numbers, it is important not to round numbers until right at the end, as small changes can be amplified by your calculations.

Step Five: It is good practice to total everything after you've finished making sure the numbers make sense

*e.g.* 3.5 ml/hour (Milk) + 0.63 ml/hour (Lipid) + 3.56 ml/hour (Aqueous) = 7.69 ml/hour
7.7 ml/hour x 24 (hours) = 184.56 ml/24 hours
184.8 ml/24 hours ÷ 1.23 (kg) = 150.05 ml/kg/24 hours

**Appendix VI:**



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| | | | | |
|---|---|---|---|---|
| Reference Number<br><br>CG-NICU/3181/22 | Version: | | Status<br><br>Final | |
| Version / Amendment History | Version | Date | Author | Reason |
| | 1 | April 2022 | | Updated in line with national guidelines |
| | 1.2 | Feb 2025 | Lisa Taylor | Change to presentation options for full PN to use off-the-shelf products. Modifications to lipid details (section 1.5, protection from light; section 1.6 table, presentation options for PN; and Lipid section of appendix I Process for QHB NNU removed as no longer required |
| Intended Recipients: Neonatal team RDH and QHB | | | | |
| Training and Dissemination: Education lead by Senior Neonatal Clinical Nurse Educator. Emails, posters and worked examples shared with the team across site. Notice board present on NNU/NICU areas with updates on new policy. | | | | |
| Development of Guideline: Harriet Hughes, Shalini Ojha<br>Job Title: Advanced Pharmacist, Women's and Children's, Neonatal Consultant | | | | |
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| | |
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