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

Reference no.:CG-NICU/3181/22

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Significant changes from previous guideline:

- Guideline merged with Queens Hospital Burton
- Lipids to be infused over 24 hours instead of 20 hours. There is no rationale for this practice, which has been abandoned by almost every other NICU. Ostensibly it was to allow for lipid-free blood samples to be taken, but we take blood samples at other times of the day and treat the results no differently. Infusing the lipids over a longer time should improve tolerance as the hourly rate is lower.
- Clarification of PN rate titration calculation given that lipids are now infused over 24 hours at RD.
- Inclusion of Numeta as a 2nd line neonatal PN[1] to improve robustness of supply to UHDB.

- Minor changes to UHDB PN order sheet to allow for rate titration based on changes to infants' fluid allowance.
- Removal of Term Regimen section of guideline as usage does not justify the relatively high level of wastage of stock.

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:

GA	Gestational Age
NBM	Nil by mouth
PN	Parenteral Nutrition
TPN	Total Parenteral Nutrition
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

[1] PN replaces the traditional TPN (total parenteral nutrition), because it is recognised that it is often used as a supplement to enteral feeding, not a complete replacement. TPN will be used to refer to situations where no enteral feeding is expected *i.e.* NBM.

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 43%, glucose reduced by 27%, total energy reduced by 21%).
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 0.22micron filter; the lipid syringe must be used with a filter size of no less than 400microns allow lipid molecules to pass through. The lipid must be changed every 24 hours.

1.5 Protect from light

Both the aqueous and lipid parenteral nutrition solutions should 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 and light protective lines. The lipid is supplied in tinted 50mL UV protect syringes. The aqueous bag is supplied in a light protective bag.

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. Where possible, white ITH Pharma bag covers will be used to protect the aqueous PN and lipids will be supplied in light protective PVC syringes.

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

Full 'TPN' is presented in two phases, commonly described as the 'aqueous phase' and the 'lipid phase'.

Aqueous Bag	600mL bag (in light protective bag)	Contains proteins (amino acids) and glucose, with added electrolytes, water sodium vitamins and trace elements as appropriate.
Lipid Syringe	50mL syringe (in amber tinted syringe)	

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, 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 3rd 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 (Early PN)
2. Preterm (Full PN)
3. Peripheral (Full PN)

All of these PN regimens are pre-made; additions can be added to Preterm and Peripheral bags **only**.

Phases of parenteral nutrition

Early PN – This phase 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 usually contains only dextrose, amino acids and calcium, but not sodium, potassium, magnesium, or phosphorus.

Full PN – This phase 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 48-72hours 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 and NNU 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 supplied by central aseptic unit (CASU) in pharmacy at RDH site for both NICU at RDH and NNU at QHB. 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, water soluble vitamins and trace elements) and the bespoke volume lipid syringe (containing lipids and fat-soluble vitamins). Sodium, potassium and phosphate may be added to this regimen if the infant's blood results indicate that this is necessary, and vitamins and trace elements are routinely added.

Peripheral PN
Peripheral PN is available 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. Therefore, it should be reserved for when central IV access is deemed inappropriate *e.g.* suspected line sepsis. Sodium, potassium and phosphate may be added to this regimen if the infant's blood results indicate that this is necessary, and vitamins and trace elements are routinely added.

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 3-5 mmol/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; 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 9mmol in 600mL).

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 1.88mmol/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 defaults to provide this ratio where possible.

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 is 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 added to 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 solution. However, as full vitamins can be added to as little as 0.5g lipid/kg/day, this is rarely necessary as most infants should receive some lipid.

Trace elements
A full range of trace minerals and electrolytes are added to give a complete feed. The trace mineral solution, Peditrace® is routinely added along with 0.2mmol/kg Mg as magnesium sulphate. 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 needs 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

Preterm PN is supplied by central aseptic unit (CASU) in pharmacy at RDH site for both NICU at RDH and NNU at QHB.

The ward pharmacist for NICU/NNU should use the central/peripheral 48 hour PN prescription which can be found on Q Pulse. Once the prescription is agreed with the neonatal registrar or consultant on the ward, the prescription requires sending to CASU at RDH.

CASU will manufacture any PN required for babies on NICU or NNU the same day as requested, so long as the finalised PN prescription is received by 1pm (latest).

<u>Process for RDH:</u>
Ward pharmacist to bring signed prescription to CASU by 1pm latest and hand over to chief technician.
Once PN manufactured and released, CASU will organise collection with NICU.
As the prescription is a 48 hour prescription, ward pharmacist will need to inform CASU whether or not the lipids are required on day 2 of the prescription.

<u>Process for QHB:</u>
Ward pharmacist to contact central aseptic unit on 01332 785344 to inform them of PN request by 1pm latest. Chief technician will provide appropriate email address to send scanned copy of signed prescription to. Ward pharmacist will need to provide CASU with their contact details should there be any questions from the aseptic team with regards to the prescription content.

Once PN manufactured and released, CASU will organise for a taxi to collect PN from the pharmacy department at RDH to be delivered to NNU at QHB. PN may arrive between the hours of 5pm – 7pm depending on CASUs workload and factors affecting transport time.

To avoid unnecessary expenditure on taxi services, CASU will make both lipid syringes on day 1 for NNU babies at QHB, so that deliveries to QHB are on alternate days.

<u>Process for Weekends:</u>
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 day time for CASU to make and supply Monday and Tuesdays PN. Any questions, contact CASU before midday on a Friday.

Any babies identified as needing PN after 1pm on a Friday, 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. If a baby is identified early on a Friday afternoon as needing PN, CASU may be able to prepare e.g. one 48 hour bag if workload allows, but this is by no means guaranteed and must be discussed with CASU at earliest opportunity.

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

Per 100ml	Starter PN	Preterm PN	Peripheral PN	Numeta G13%[2]
Protein[3]	3.5g	2.9g	1.7g	3.1g
Glucose	15g	12.5g	9.2g	13.3g
Lipid	×	2.5g	2.5g	2.5g
Sodium	×	2.9mmol	2.5mmol	2.2mmol
Electrolyte additions	×	✓	✓	✓
Vitamins	×	✓	✓	✓
Trace elements	×	✓	✓	✓
Stock on NICU	✓	×	×	×
Route of administration	Central	Central	Peripheral	Central
Bag volume	160ml	610ml	500ml	300ml
Maximum rate	80ml/kg/day	120ml/kg/day	120ml/kg/day	127.9ml/kg/day
When to be used	Up to 72hours of age	From 24hrs of age	From 24hrs 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 0.22micron filter.

Starter PN

Volume	/kg/day	10ml/kg	20ml/kg	30ml/kg	40ml/kg	50ml/kg	60ml/kg	70ml/kg	80ml/kg
Protein	g	0.35	0.7	1.05	1.4	1.75	2.1	2.45	2.8
Glucose	g	1.5	3	4.5	6	7.5	9	10.5	12
Fat	g	0	0	0	0	0	0	0	0
Energy	Kcal	7	15	22	30	37	44	52	59
Na^+	mmol	0	0	0	0	0	0	0	0
K^+	mmol	0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.8
Ca^{2+}	mmol	0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.8
Mg^{2+}	mmol	0.02	0.04	0.06	0.08	0.1	0.12	0.14	0.16
PO_4^{3-}	mmol	0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.8

Preterm PN (with 3g/kg/day lipid)

Volume	/kg/day	40ml/kg	50ml/kg	60ml/kg	70ml/kg	80ml/kg	90ml/kg	100ml/kg	110ml/kg	120ml/kg
Protein	g	1.2	1.5	1.8	2	2.3	2.6	2.9	3.2	3.5
Glucose	g	5.0	6.3	7.5	8.8	10.0	11.3	12.5	13.8	15
Fat	g	1	1.3	1.5	1.8	2	2.3	2.5	2.8	3
Energy	Kcal	35	43	52	61	69	78	87	95	104
Na^+	mmol	1.2	1.5	1.8	2	2.3	2.6	2.9	3.2	3.5
K^+	mmol	0.8	1	1.3	1.5	1.7	1.9	2.1	2.3	2.5
Ca^{2+}	mmol	0.7	0.8	1.0	1.2	1.3	1.5	1.7	1.8	2
Mg^{2+}	mmol	0.07	0.08	0.1	0.12	0.13	0.15	0.17	0.18	0.2
PO_4^{3-}	mmol	0.8	0.9	1.1	1.3	1.5	1.7	1.9	2.1	2.25

[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.

[3] PN doesn't contain protein *per se* (which would most likely be immunogenic, not to mention unusable by the body), but the amino acid content of PN is often expressed as g of protein or g of nitrogen (N). To say that Starter PN contains 3.5g of protein per 100ml indicates that 100ml contains amino acids equivalent to 3.5g protein.

Peripheral PN (with 3g/kg/day lipid)

Volume	/kg/day	40ml/kg	50ml/kg	60ml/kg	70ml/kg	80ml/kg	90ml/kg	100ml/kg	110ml/kg	120ml/kg
Protein	g	0.7	0.8	1	1.2	1.3	1.5	1.7	1.8	2
Glucose	g	3.7	4.6	5.5	6.4	7.3	8.3	9.2	10.1	11
Fat	g	1	1.3	1.5	1.8	2	2.3	2.5	2.8	3
Energy	Kcal	27	34	41	48	55	62	68	75	82
Na^+	mmol	1	1.3	1.5	1.8	2	2.3	2.5	2.8	3
K^+	mmol	0.8	1	1.3	1.5	1.7	1.9	2.1	2.3	2.5
Ca^{2+}	mmol	0.3	0.4	0.5	0.6	0.7	0.8	0.8	0.9	1
Mg^{2+}	mmol	0.07	0.08	0.1	0.12	0.13	0.15	0.17	0.18	0.2
PO_4^{3-}	mmol	0.8	0.9	1.1	1.3	1.5	1.7	1.9	2.1	2.3

Numeta (3CB)

Volume	/kg/day	20ml/kg	30ml/kg	40ml/kg	50ml/kg	60ml/kg	70ml/kg	80ml/kg	90ml/kg	96.2ml/kg
Protein	g	0.52	0.78	1.04	1.3	1.56	1.82	2.08	2.34	2.5
Glucose	g	3.1	4.7	6.2	7.8	9.3	10.9	12.4	14.0	14.9
Fat	g	0.6	0.9	1.2	1.6	1.9	2.2	2.5	2.8	3
Energy	Kcal	21	31	41	52	62	72	82	93	99
Na^+	mmol	0.5	0.7	1	1.2	1.4	1.7	1.9	2.2	2.3
K^+	mmol	0.5	0.7	0.9	1.2	1.4	1.6	1.8	2.1	2.2
Ca^{2+}	mmol	0.12	0.19	0.25	0.31	0.37	0.43	0.5	0.56	0.6
Mg^{2+}	mmol	0.06	0.09	0.12	0.16	0.19	0.22	0.25	0.28	0.3
PO_4^{3-}	mmol	0.17	0.26	0.35	0.44	0.52	0.61	0.7	0.78	0.84

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 and may need supplementing, whereas calcium and phosphate are elevated – these may not prove problematic but should be monitored and if they are elevated then aqueous PN rate can be reduced down 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	15	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

[4] Including glucose from 10% glucose infused separately to top up fluids
[5] As lipids are run at full rate

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 400microns, 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. 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 preterm bag:

Amino acids
Amino acids are provided by Vaminolact, which is comprised of the following:

Amino acid	**per 100ml**	**Amino acid**	**per 100ml**
Glutamic acid	710mg	Isoleucine	310mg
Leucine	700mg	Phenylalanine	270mg
Alanine	630mg	Glycine	210mg
Lysine	560mg	Histidine	210mg
Proline	560mg	Tryptophan	140mg
Arginine	410mg	Methionine	130mg
Aspartic acid	410mg	Cysteine	100mg
Serine	380mg	Tyrosine	50mg
Threonine	360mg	Taurine	30mg
Valine	360mg		

[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.

Composition of Vitamin and Trace Mineral Additives

Water soluble vitamins – Solivito N

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®

4 ml/kg (to a maximum daily dose of 10 ml/day) is added to the lipid

Infants ≤ 2.5 kg will receive 4 ml/kg, 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 will receive 10 ml daily, providing a total daily intake of:

Vitamin A	690 micrograms (2300 units)/day
Vitamin D	10 micrograms (400 units) /day
Vitamin E	6.4 mg (7 units) /day
Vitamin K	200 micrograms/day

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

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 2:1 in Preterm regimens. This ratio has been shown to promote good nitrogen retention[ii]. Increasing carbohydrate and/or fat could provide more energy if required but advice must be taken from a neonatal dietician or neonatal pharmacist. Any regimen requiring more or less carbohydrate would have to be out sourced (i.e. manufactured by another

aseptic unit within the region). This would be at consultant request only. 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.

Glucose

Starter PN and the aqueous bag of Preterm PN both contain 15% 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 the aqueous portion of PN, so g/kg/day (or mg/kg/min may be more appropriate). See Appendix I/11 (see trust specific appendix) for glucose intake of different PN Regimens at different rates.

Lipid

The lipid provided is Intralipid 20%, a purified soybean oil emulsion, which is isotonic. This provides energy, essential fatty acids and a small quantity of organic phosphate. The phosphate content of Intralipid is 15mmol/L[iii], 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[iv]. Levels up to 3g/kg/day have been shown to be tolerated when infused over 24 hours[v,vi,vii], though infants born weighing <1kg are less likely to tolerate even 3g/kg/day[viii]. 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			

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

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 × 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.

The lipid component accounts for ~15% of the volume of the total PN, so multiply the hourly rate by 0.15.

E.g. for Lipid bag Rate: 4.1ml/hour x 0.15 = 0.615 ml/hour therefore 0.6 ml/hour (rounded to 1 d.p)

The aqueous component accounts for ~ 85% of the volume of the total PN, so multiply the hourly rate by 0.85.

E.g. for Aqueous bag Rate: 4.1 ml/hour x 0.85 = 3.485 ml/hour therefore 3.5 ml/hour (rounded to 1 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. 0.6 ml/hour (Lipid) + 3.5 ml/hour (Aqueous) = 4.1 ml/hour.
4.1 ml/hour (PN) × 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.

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/24hours = 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.

The Lipid component accounts for ~15% of the volume of the total PN, so multiply the new hourly rate by 0.15.

e.g. 3.85 ml/hour x 0.15 = 0.6 ml/hour (rounded to 1 d.p)

The Aqueous component accounts for ~ 85% of the volume of the total PN, so multiply the hourly rate by 0.85.

e.g. 3.85 ml/hour x 0.85 = 3.3 ml/hour (rounded to 1 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) + 0.6 ml/hour (Lipid) + 3.3 ml/hour (Aqueous) = 4.65 ml/hour
4.65 ml/hour x 24 (hours)= 111.6 ml/24 hours
111.6 ml/24 hours ÷ 1.23kg = 90.7 ml/kg/24 hours

cenario 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 = 7.68 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. 7.68 ml/hour – 6.15 ml/hour – 0.5ml/hour = 1.0 ml/hour (to 1 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)

The Lipid component accounts for ~ 15% of the volume of the total PN, so multiply the new hourly rate by 0.15.

e.g. 6.15 ml/hour x 0.15 = 0.9 ml/hour (rounded to 1 d.p)

The Aqueous component accounts for ~ 85% of the volume of the total PN, so multiply the hourly rate by 0.85.

e.g. 6.15 ml/hour x 0.85 = 5.2 ml/hour (rounded to 1 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) + 0.9 ml/hour (Lipid) + 5.2 ml/hour (Aqueous) = 7.6 ml/hour
7.6 ml/hour x 24 (hours) = 182.4 ml/24 hours
182.4 ml/24 hours ÷ 1.23 kg = 148.3 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)

The Lipid component accounts for ~ 15% of the volume of the total PN, so multiply the new hourly rate by 0.15.

e.g. 4.19 ml/hour x 0.15 = 0.6 ml/hour (rounded to 1 d.p)

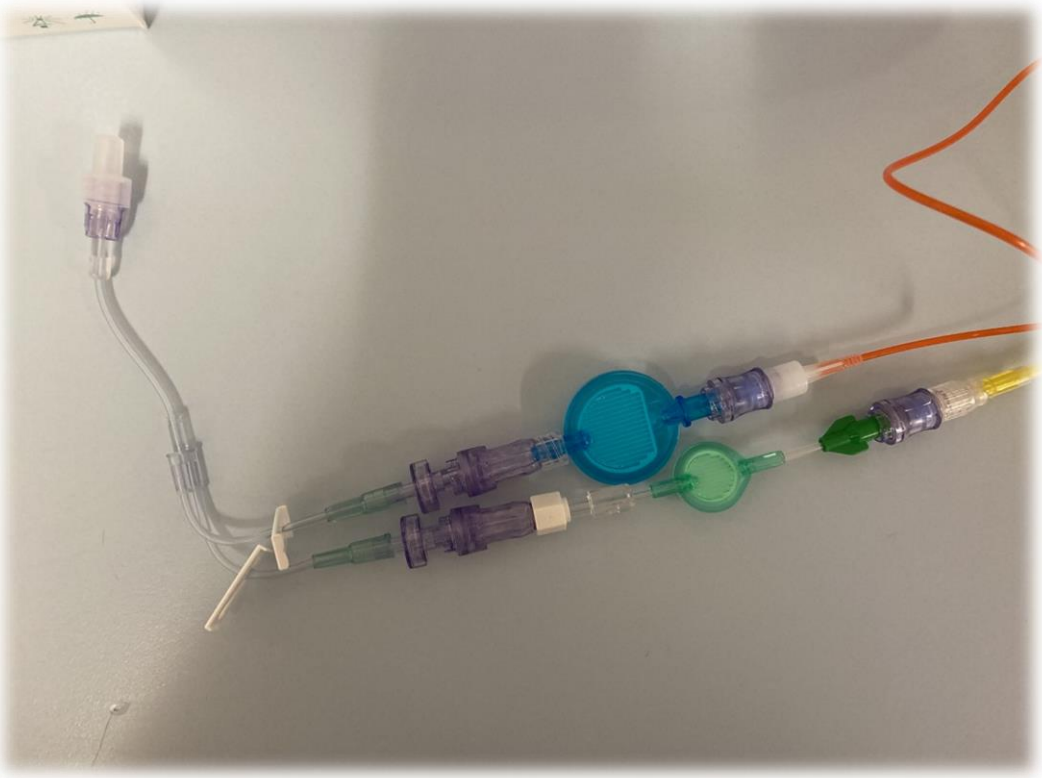
The aqueous component accounts for ~ 85% of the volume of the total PN, so multiply the hourly rate by 0.85.

e.g. 4.19 ml/hour x 0.85 = 3.6 ml/hour (rounded to 1 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) + 0.6 ml/hour (Lipid) + 3.6 ml/hour (Aqueous) = 7.7 ml/hour
7.7 ml/hour x 24 (hours) = 184.8 ml/24 hours
184.8 ml/24 hours ÷ 1.23 (kg) = 150.2 ml/kg/24 hours

Appendix VI:



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				Updated in line with national guidelines
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Development of Guideline: Harriet Hughes, Shalini Ojha Job Title: Advanced Pharmacist, Women's and Children's, Neonatal Consultant				
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