East of England Neonatal ODN
(Hosted by Cambridge University Hospitals)

# Clinical Guideline:
# Parenteral Feeding of Infants on the Neonatal Unit.

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Original guideline developed in conjunction with the East of England ODN Neonatal Nutrition Working Group (2013).

**For use in:** EoE Neonatal Units
Guidance specific to the care of neonatal patients.

**Used by:** Medical Staff, Neonatal Nurse Practitioners, Dietitians, Pharmacists

**Key Words:**

| | |
|---|---|
| PN | Parenteral Nutrition |
| GOR | Glucose Oxidation Rate |
| EFA | Essential Fatty Acid |
| SMOF | Soya, Medium chain, Olive oil, Fish oil intravenous lipid blend |
| ESPGHAN | European Society of Paediatric Gastroenterology, Hepatology & Nutrition |
| NEC | Necrotising Enterocolitis |
| UVC | Umbilical Venous Catheter |
| AREDF | Absent/ Reduced End Diastolic Flow |
| VLBW | Very Low Birth Weight Infant |
| ELBW | Extremely Low Birth Weight Infant |
| NCEPOD | National Confidential Enquiry into Patient Outcome and Death |
| PNALD | Parenteral Nutrition Associated Liver Disease |
| IUGR | Intra-Uterine Growth Retardation |
| IVC | Inferior Vena Cava |
| SVC | Superior Vena Cava |
| PAU | Pharmacy Aseptic Unit |

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**Approved by:**

| | |
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| Neonatal Clinical Oversight Group | |
| Clinical Lead Matthew James | **Matthew James** |

**Ratified by ODN Board:**

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| **Date of meeting** | |

**Audit Standards:**

- 100% infants meeting the absolute indicators within the prescribing criteria commence parenteral nutrition within 8 hours of the decision to commence PN
- 100% infants meeting prescribing criteria receive a minimum of 1.5 – 2.0g/kg/day amino acid on day 1 of PN.
- 100% infants receive standardised PN accurately prescribed using the East of England PN prescribing proformas, and where deviation from standardised PN occurs the reason for this deviation is clearly recorded in the patient's medical notes.
- 100% infants receive both aqueous and lipid PN that has all components protected from light.
- 100% units have access to a nutrition MDT that comprises at a minimum a Consultant Neonatologist/Paediatrician with an interest in neonatology, a neonatal dietitian and a neonatal pharmacist.

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## 1.0 Introduction

Early postnatal growth failure, with associated longer-term neuro-developmental implications, is frequently encountered in very premature infants and is most evident in the smallest, sickest infants (1). Multi-factorial in origin (2), postnatal growth failure can be considered, in part, due to inadequate nutritional intake in the first four weeks after delivery and, although long term neuro-cognitive outcomes are lacking, recent studies have demonstrated that optimising nutrition within the first four weeks of life improves both head and somatic growth. (3)
Delivery of intravenous nutrients, as parenteral nutrition, dominates the nutritional management of very premature infants whilst enteral feeds are being established, as well as in more mature infants with gastrointestinal malformation or impairment. In both groups in order to minimise the growth failure and neuro-cognitive effects of early nutrient deficit, the development of strategies for effective PN delivery are essential.

A 2010 case review of neonates who received parenteral nutrition highlighted large variations in neonatal PN quality and practice throughout the UK, with the provision of early PN deemed inadequate in a third of infants and PN monitoring inadequate in a fifth. The commencement of PN was delayed in 45% of cases reviewed either because the need went unrecognised or was not acted upon. (4)

A further report from the Chief Pharmacists in 2011 identified concerns regarding the prescribing and administration of neonatal PN and highlighted that in order for PN to be successful, agreed guidelines that are both based on and referenced to published evidence need to be in place.(5) Relevant clinical indications, nutrient requirements and mode of delivery also need to be clearly defined.(6) The subsequent publication of guidelines and frameworks for practice, developed by the National Institute for Health and Clinical Excellence (NICE) in 2020, (7) the European Society of Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) in 2018 (8) and the British Association of Perinatal Medicine (BAPM) in 2016 (9) seek to establish a framework for the provision of appropriate PN for preterm infants and children. These frameworks form the basis of this document and as such are intended to serve as an aid to clinical judgement and not as a replacement.

## 2.0 Indications for Parenteral Nutrition

Premature infants are born with an immature gut consequently the smallest infants are unable to digest sufficient milk to meet their nutritional requirements. They are also born with low nutritional reserves (10) such that a 1 kg infant will become deficient in essential fatty acids within 2 days of birth and survive only 4 days if not provided with appropriate nutrition (11 12). Virtually all preterm infants <30 weeks gestation will require parenteral nutrition for a period of time, the duration of which is determined by gestation, birth weight and other concurrent morbidities.
NICE recommend PN be commenced in all infants <31 weeks gestation (7), however amending the EOE guidance absolute indicator to all infants <31 weeks will increase network PN usage by up to 35%. As evidence for the timeframes for provision of PN is extremely limited, the NICE recommendation was based on expert committee consensus only. Considering the impact this amendment to criteria would have on the wider health economy and the poor quality evidence supporting the recommendation, there would seem little clear justification for changing the current EOE recommendations at the present time.
Parenteral nutritional support in the preterm infant should commence as soon as possible after the decision to give PN is made. NICE recommend at the latest within 8 hours of the decision to start (7) whilst ESPGHAN recommend PN be commenced as soon as possible and definitely within 24 hours (9). Table 1 provides some indications for neonatal PN prescribing, however any neonate who has

not progressed and who is unlikely to have established enteral feeding within 72 hours of birth should be considered for PN (7).

Table 1: Indications for PN in Neonates

| | |
|---|---|
| Absolute Indications | Premature infants < 30 weeks gestation or <1.25kg<br>Intestinal Failure (i.e. short gut, pseudo-obstruction)<br>Gastrointestinal Surgery<br>Necrotising Enterocolitis (NEC)<br>Congenital gastrointestinal defects (i.e.gastroschisis, intestinal atresia) |
| Relative Indications | Any infant ≥30 weeks' gestation or >1.25kg who has not progressed and is unlikely to have established enteral feeding within 72 hours of birth.. |

Indications for PN in an infant previously established on enteral feeds.

Preterm, and to a lesser extent, term infants, have limited nutritional stores and therefore there is a potential for accumulated nutritional deficits should enteral nutrition stop. PN should be considered for any neonate previously on enteral feeds where the re-establishment of adequate enteral feeding within 2-3 days is unlikely.

**Recommendation**

- For **preterm and term infants** Parenteral Nutrition (PN) should be commenced as soon as the decision to provide has been made. This should be within 8 hours and definitely within 24 hours in any infant that meets the specified criteria.
- PN should be commenced for **preterm infants** previously established on enteral nutrition when either feeds have to be stopped and are unlikely to restart within 48 hours, or where feeds have already been stopped for >24 hours and there is unlikely to be sufficient progress with advancing feeds within the next 48 hours.
- PN should be commenced for **term infants** previously established on enteral nutrition when either feeds have to be stopped and are unlikely to restart within 72 hours, or where feeds have already been stopped for >48 hours and there is unlikely to be sufficient progress with advancing feeds within the next 48 hours.

## 3.0 Parenteral nutritional for Neonates

## 3.1 Fluid and Electrolyte Requirements

Immediately after birth the adaptation process of water and electrolyte metabolism commences and therefore is intrinsically linked to the early stages of PN delivery. The process occurs in 3 phases and is characterised by rapid changes in both intracellular and extracellular body compartments (8)

**Phase I** – Transition: initial oliguria lasting hours – days, plus considerable insensible water losses from the immature skin. This is followed by a diuretic phase usually associated with up to 10% weight loss. Extremely low birth weight (ELBW) infants are liable to early excess water losses and may become dehydrated without meticulous attention to early fluid balance.
**Phase II**: - Intermediate; the phase between an infant's lowest weight and a return to birth weight. During this phase electrolyte losses decrease and levels are repleted, although on occasion urinary output can still be high with high sodium excretion, especially in ELBW/VLBW infants.
**Phase III**: - The stable growth phase with a positive net balance of sodium and water.

Account should be taken of insensible losses and influencing environmental factors when determining fluid requirement for preterm infants, especially in the first week of life (13). For the majority of stable infants, fluid requirements are relatively predictable and can be accurately managed with a stepwise introduction of standardised PN solutions over 3-4 days.

In some situations total fluid allowance may be restricted or a proportion of the volume required for other infusions. In order to minimise the resultant risks of compromised nutritional provision standardised PN formulations should be compounded in the smallest volume possible, as concentrating PN will facilitate the provision of nutritional requirements within the total fluid allowance (7).

Sodium and potassium

Sodium and potassium should be given in PN to maintain standard daily requirements (7) and can be safely given from the first day of life, especially when giving recommended levels of amino acid and energy (8).Where required, additional supplements of sodium and potassium should ideally be given as separate infusions rather than as additions to the PN bag in order to facilitate the provision of maintenance electrolytes within the standardised PN formulation. (7). It is important to note that sodium will also, by necessity, be present in conjunction with phosphate delivery and that high levels of sodium may be delivered in non – PN infusions, medications and flushes.

Chloride

Chloride intake should be lower than the combined sodium and potassium intake in order to reduce the risk of iatrogenic acidosis.

Parenteral Fluid Requirements for the Premature Infant (8)

| | **<1000g (ml/kg/day)** | | **1000-1500g (ml/kg/day)** | | **>1500g (ml/kg/day)** |
|---|---|---|---|---|---|
| Day 1 | 80-100 | Day 1 | 70 – 90 | Day 1 | 60-80 |
| Day 2 | 100-120 | Day 2 | 90-110 | Day 2 | 80-100 |
| Day 3 | 120-140 | Day 3 | 110-130 | Day 3 | 100-120 |
| Day 4 | 140-160 | Day 4 | 130-150 | Day 4 | 120-140 |
| Day 5 | 160-180 | Day 5 | 160-180 | Day 5 | 140-160 |

| Parenteral Electrolyte Requirements for infants (8) | **Day 1 Mmol/kg** | **Day 2 Mmol/kg** | **Day 3 Mmol/kg** | **Day 4 Mmol/kg** | **Day 5 Mmol/kg** |
|---|---|---|---|---|---|
| **Sodium** | | | | | |
| | | | | | |
| <1500g infant | 0-2(3) | 0-2(3) | 0-5(7) | 2-5(7) | 2-5(7) |
| >1500g | 0-2(3) | 0-2(3) | 0-3 | 2-5 | 2-5 |
| Term infant<br>no daily recommendation | 2-3 | | | | |
| **Potassium** | | | | | |
| All premature infants | 0-3 | 0-3 | 0-3 | 2-3 | 2-3 |
| Term infant<br>no daily recommendation | 1-3 | | | | |
| **Chloride** | | | | | |
| All premature infants | 0-3 | 0-3 | 0-3 | 2-5 | 2-5 |
| Term infant | No recommendation | | | | |

**Recommendations**

- Standardised PN formulations should be compounded in the smallest possible volume to allow provision of nutritional requirements.

- The contribution of intravenous medication and flushes should be considered when determining sodium requirements for PN.
- Sodium and potassium can be given from the first day of life especially when recommended amino acid and energy intakes are provided. The needs of individual infants may deviate markedly from the recommended ranges depending on clinical condition. Additional sodium and potassium should ideally be provided as separate intravenous infusions alongside standardised PN bags.

## 3.2 Energy Requirements

Due to the preterm infant's limited nutritional stores the goal is to initiate nutrition support as soon as possible and achieve early energy accretion (14). A number of studies have demonstrated that the provision of adequate quantities of protein and energy can significantly improve postnatal growth in preterm infants (15-19), however it must be born in mind that a number of conditions and treatment (including medication) can affect the energy needs of preterm infants and as such should be always be considered when assessing energy requirements (table 2).
In recognition of the early metabolic adaptation that occurs in the first few days of life energy provision should be increased gradually in infants receiving PN within the first 4 days after birth. Those commencing PN after day 4 of life can be assumed to have completed early metabolic adaptation so PN can commence at maintenance range (7).

Energy requirements of preterm infants should cover the i) energy needs for basal metabolic functions (BMR), ii) energy expended for physical activity, iii) diet induced thermogenesis, iv) energy for new tissue growth and v) energy loss in stool and urine. As BMR is hard to measure, resting energy expenditure (REE) is usually estimated instead, for neonates this figure includes diet-induced thermogenesis as they are rarely strictly in a fasting state.(20)

Energy expenditure in most preterm infants commences at around 35-55Kcal/Kg/day and increases over the first two weeks of life to about 70kcal/kg/day by one month of age(for term infants this is 45-50Kcal/kg/day increasing to 60Kcal/kg/day by one month)(20). . Energy requirements for growth are 3-5Kcal/g/day. Very preterm infants will therefore have an additional energy need of 50-70Kcal/kg/day, suggesting a total enteral energy intake of up to 120/kg/day is required to facilitate maximal protein accretion and approximate intrauterine growth, 30 - 40Kcal/kg/day with a total of up to 90Kcal/kg/day for term infants. (20) Since the amino acid component of PN is required for tissue repair and new tissue synthesis, the majority of energy provided in PN should be from the non-nitrogen sources (ie lipid and carbohydrate).(9) As this is a theoretical prediction consideration should be given to the factors in the table below, as well as anthropometric and biochemical monitoring parameters when reviewing and assessing energy needs.

Table 2 Factors that may impact on energy requirements of the neonate. (21-24)

| Factor | Comment |
|---|---|
| Physical activity | Activity is estimated to be 10% of a preterm infant's total energy requirements. This figure is reduced if the baby is ventilated, sedated and on muscle relaxants |
| Feeding | The thermic effect of food is 10% if bolus feeds are given. The effect is negligible with PN and continuous enteral feeding. |
| Human milk | Non-nutritive factors aid absorption thereby reducing the energy required for digestion |
| Prematurity | Gestational age is negatively correlated with energy expenditure |
| Excessive energy intake | Increases thermogenesis and the production of $CO_2$ |
| Weight gain | Energy requirements require adjustment as the child grows. |
| Mechanical ventilation | Depending on ventilation mode and pressure support there is either no effect or a reduction in energy expenditure. |
| Nasal CPAP | Reduces work of breathing thereby reducing energy expenditure. |
| Thermal environment | Both cold and heat can increase energy requirements. |

| | |
|---|---|
| Chronic Lung Disease | Increases work of breathing which leads to higher $O_2$ requirements, increased $CO_2$ production and increased energy expenditure. |
| Sepsis | No clear evidence. Some studies have indicated no change in energy expenditure, some a reduction. |
| Surgery/ NEC | Evidence is equivocal |

**Recommendations**

- For **preterm and term infants**, if starting PN within the first 4 days of life give a starting range of 40-60Kcal/kg/day gradually increasing over a small number of days
- Most **preterm infants** will meet their energy requirements and approximate intra-uterine lean body mass and growth rates when provided with a maintenance level of up to 120Kcal/kg/day
- Most **term infants** will meet their energy requirements and approximate intra-uterine lean body mass and growth rates when provided with a maintenance level of up to 90Kcal/kg/day
- For **preterm and term infants**, if starting PN more than 4 days after birth give maintenance levels from the first day of PN
- Factors that may reduce/increase requirements should be taken into account when estimating an individual infant's requirement.

## 3.3 Amino acid Requirements

Early introduction of amino acids is essential in the preterm infant if the high accretion rates seen in foetal life are to be matched and the large deficits found in the first week of life are to be avoided. (25) Provision should commence on the first day of life as current evidence suggests it is safe to commence amino acid provision immediately from birth onwards without metabolic complications (25-29)

Estimates of amino acid requirements in preterm infants are based on the quantity required to achieve a positive nitrogen balance. The preterm infant excretes between 0.6-1.1 g/kg protein per day such that an amino acid intake of 0.9g/kg/day is required to prevent significant loss (30). In the presence of adequate non nitrogen energy a positive nitrogen balance can be achieved with an amino acid intake 0.9 – 2.65g/kg/day (31,8).

Variations in the design of amino acid studies makes interpretation and the identification of recommended levels of intake challenging. A recent Cochrane Review concluded that higher parenteral AA intakes do not affect mortality and could reduce the incidence of postnatal growth failure and retinopathy of prematurity. However, in some infants higher AA intakes were associated with potentially adverse biochemical effects resulting from excess amino acid loads. Evidence was also insufficient to show whether higher AA intake had an effect on neurodevelopment (34).

Available evidence does however suggest that nitrogen balance is not improved by starting doses >3.5g/kg when compared to starting doses of 1.5-2.4g/kg/day (9,24,26).
There is still limited evidence that increasing target amino acid intake >2.5g/kg/day is associated with a more favorable outcome. Some studies suggest that intakes of 3.5-4.0g/kg/day (with adequate non nitrogen energy) are associated with improved growth outcomes (3,33,34). In contrast there is some evidence of appropriate growth at maximal parenteral intakes of 2.7g/kg/day, but this was in association with early (within 24 hours) and progressive enteral nutrition. (35).
ESPGHAN and NICE both recommend that amino acid should commence with at least 1.5g -2.0g amino acid/kg/day in order to achieve an anabolic state (7 8) gradually increasing to a maintenance range of 3-4g/Kg/day (7) or e 2-5-3.5g amino acid/kg/day alongside adequate non nitrogen energy > 65Kcal/kg/day. (8)
The ratio of energy: amino acid in PN almost certainly affects the utilisation of amino acids and it is generally accepted that 30-40Kcal/g amino acid (20-30 non-nitrogen Kcal/g) is needed to optimise protein uptake (7), with a daily provision of up to12Kcal total energy/kg/day required for optimal

protein accretion in preterm infants (20). These values are supported by studies that evaluated the effect of different amino acid doses on the growth and amino acid profiles of preterm infants (36). The levels of energy glucose and lipid that provide optimal protein accretion and growth has yet to be determined. (3 7 37) however there are risks associated with providing too high or too low a ratio. Too low (<20Kcal/g amino acid) can cause oxidation of amino acids and high blood urea, whereas too high a ratio (>30Kcal/g amino acid) could result in deposition of excess body fat with the possibility of metabolic ill health in later life.

There is little evidence about the amino acid requirements of term infants. Term infants appear to lose less protein than preterm infants, it is therefore suggested that the amount of amino acid in term PN should reflect the amounts needed to achieve similar weight gain in infants receiving milk feeds.(7)

The amino acids taurine cysteine and tyrosine are considered semi-essential during the neonatal period. It is therefore important to use amino acid solutions in neonatal PN that have been specifically manufactured to meet the needs of this population.

**Recommendation**

- Where a decision is made to give PN, amino acid provision should commence within 8 hours of that decision being made.
- In **preterm infants** amino acid provision should commence at 1.5 – 2.0g /kg/day on the first day increasing to 3.0 – 4.0g/kg/day.
- If commencing PN more than 4 days after birth for a **preterm infant** give a range of 3.0 - 4.0g amino acid/Kg/day from day 1.
- In **term infants** amino acid provision should commence at 1.0 – 2.0g /kg/day on the first day increasing to 2.5 – 3.0g/kg/day.
- If commencing PN more than 4 days after birth for a **term infant** give a range of 2.5 - 3.0g amino acid/Kg/day from day 1.
- An energy:amino acid ratio of 30-40Kcal/g amino acid (20-30 non-nitrogen Kcal/g amino acid) is required for effective utilisation of protein.
- Amino acid solutions specifically designed for neonates and containing cysteine, tyrosine and taurine should be used for compounding PN for preterm and term infants.

## 3.4 Carbohydrate Requirements

Carbohydrate in PN is prescribed as glucose. It serves as the primary source of energy for the brain, renal medulla and erythrocytes and as metabolic fuel for muscle, liver, heart, kidney and the gut. Glucose is the primary determinant for both glucose utilisation and the metabolism of fat (20) and is the major contributor to the osmolality of a PN solution (6,38).

Glucose recommendations are generally based on the endogenous glucose production rate (GPR) and the glucose oxidation rate (GOR). . For preterm infants this is approximately 6mg/kg/minute (8.6g/kg/day) and 8mg/kg/min (11.5g/kg/day) respectively, and for term infants 5mg/kg/min (7.2g/kg/day) and 12-12.5mg/kg/min (17.5-18g/kg/day). (20). Glucose should be increased gradually as tolerated with attention paid to glucose provided by other sources, e.g. other IV infusions.

Care must be given not to provide glucose over and above recommended rates as excess is directed to lipogenesis where glucose is converted to fat and fat oxidation ceases, thereby promoting fat deposition. Excessive glucose provision may also impair liver function by inducing steatosis. It has been suggested that high glucose feeding increases total VLDL triglyceride secretion and can also impair protein metabolism.

Hyperglycaemia is a common complication of preterm parenteral nutrition which is frequently managed with insulin infusions. The safety and effects of insulin therapy on clinical outcomes in this

population are currently unknown, therefore use should be limited to situations where reasonable adaptation of glucose infusion rate does not control hyperglycaemia (8)

**Recommendation**

- Glucose should provide 60-75% of total energy (7).
- Glucose requirements should be calculated using endogenous glucose production rates (GPR) and glucose oxidation rates (GOR) to ensure supply is within a safe range.
- For **both preterm and term infants**, if starting PN in the first 4 days after birth glucose intake should commence at 4-6mg/kg/minute (6.0-9.0g/kg/day)
- From day 2 onwards target glucose intake should be 6-11mg/kg/minute (9.0 – 16.0g/kg/day
- For **both preterm and term infants**, if starting PN more than 4 days after birth give a starting range of 6-11mg/kg/min (9.0 – 16.0g/kg/day)
- Maximum glucose infusion for long-term PN should not exceed 16g/kg/day
  Insulin infusions can be used in preterm infants with hyperglycaemia but use should be restricted to situations where reasonable adaptation of glucose infusion rates does not control hyperglycaemia.

## 3.5 Lipid Requirements

In premature infants, lipid administration is important for ensuring an increased calorie intake within a low volume and for the provision of essential fatty acids (EFA). EFA deficiency can develop within 2-3 days in the preterm infant who does not receive an adequate infusion of lipid. (39,40) Minimum essential fatty acid requirements are 0.25g/kg/day linoleic acid which are met by 0.5g[2.5ml]/kg/day Intralipid or 1.5g[7.5ml]/kg/day SMOFLipid. Total lipid requirements are based on optimal fat oxidation, which is itself linked to the supply of glucose. Maximum fat oxidation occurs when intravenous lipid emulsions provide 25-50% of a preterm infants' non protein energy requirement (8). ESPGHAN recommend a non-nitrogen energy ratio of 25-50% lipid energy : 75-50% carbohydrate energy (8), whereas NICE recommend 25-40% lipid energy : 75-60% carbohydrate energy (7)

The maximum lipid requirement for preterm and term infants is 3–4g/kg/day. (7 8)

The evidence base for the gradual introduction of lipid (starting at 1g/kg/day and increasing to 3-4g/kg/day) remains limited (7 8) though starting high doses of lipid on day 1 of life (2-3g/kg/day) may result in a higher incidence of hyperlipidaemia.(19). Practically gradual incremental increases in lipid allows for the monitoring of hypertriglyceridaemia.

The early administration of lipids (day 1-2) in the first days of life appears to be safe and well tolerated and does not appear to increase the incidence of respiratory impairment, chronic lung disease, sepsis, necrotising enterocolitis, intraventricular haemorrhage or retinopathy of prematurity in premature infants (19,41,42,43,44). There is also some evidence that shows slowly increasing lipids from a low starting dose to a target dose may be associated with a reduced risk of retinopathy of prematurity and hypertriglyceridaemia rather than rapidly increasing to the same target dose from a higher start point.(7)

Provision of 3.5g/kg/day lipid in the first week of life has been shown to be well tolerated in very low birthweight infants and associated with improved energy intakes and weight at hospital discharge (45) In smaller, extremely low birthweight infants however, hyperglycaemia may be exacerbated by higher rated of lipid infusion (19)

The optimal source of lipid for preterm infants has yet to be established. ESPGHAN suggest that infants given pure soybean oil (ie Intralipid) receive less balanced nutrition than those given composite emulsions (eg SMOFLipid) so recommend that infants likely to be in receipt of PN for "more than a few days" should be given a composite lipid emulsion containing some fish oil from the start of PN (8). In contrast a 2019 Cochrane review of intravenous lipid emulsion use in preterm infants concluded that no one lipid emulsion was any better than another for the prevention of

PNALD/cholestasis, retinopathy of prematurity or chronic lung disease. Neither were there any differences in growth, mortality, or other neonatal outcomes. (46)
NICE felt there was insufficient evidence to make any recommendation as to preferential lipid emulsions for day to day use in the neonatal unit (7).
A weak association between composite lipids emulsions and a reduction in sepsis has been described in the literature but there remains no clear evidence of either benefit or harm from their routine use in preterm infants (19,43)

**Recommendation**

- For both **preterm and term infants**, if starting PN within the first 4 days of life, Intravenous lipids should commence at 1-2g/kg/day.
- Maximum lipid provision for both **preterm and term infants** should be 3-4g/kg/day.
- Incremental introduction may reduce the risks of hypertriglyceridaemia and retinopathy of prematurity.
- Preterm infants should receive a minimum 0.25g/kg/day linoleic acid in order to prevent EFA deficiency (met by 0.5g [2.5ml]/kg/day Intralipid or 1.5g [7.5ml]/kg/day SMOFLipid).
- Lipid should provide 25-40% non-protein calories.
- 20% intravenous lipid emulsions should be first line choice for preterm infants.
- There is no evidence to support the use of one lipid emulsion over another for routine use in neonates.

## 3.6 Vitamin, mineral and trace element requirements.

### 3.6.1 Vitamins

The optimal parenteral vitamin requirements for both preterm and term infants have never been determined. Available recommendations are therefore based on expert opinion and best practice (8). Until further research is available, these will remain the recommended intakes for vitamins in neonatal PN. The adequate provision of fat and water soluble vitamins is limited by the availability of commercial preparations and is addressed in section 2 of this guidance.

An adequate supply of vitamins is essential for growth and development. As preterm infants may have low or borderline body stores of fat soluble vitamins secondary to limited cross maternal placental transfer, a sufficient supply from the first day of life is recommended. Water soluble vitamins must be administered regularly as they are not stored in any significant amounts.

Vitamins administered intravenously can adhere to delivery tubing and/or be degraded by light. As a result the actual amount delivered to the infant may be significantly lower than the intended dose. This is particularly the case with vitamin A if the fat soluble vitamins are administered in the aqueous PN, and when the infusion rate is slow.

Vitamin preparations can protect lipid emulsions from peroxidation, therefore administration of both fat and water soluble vitamin preparations with the lipid emulsion provides a practical way to limit vitamin loss and reduce lipid peroxidation.(47,48)

Recommendations:

- For **preterm and term infants** both fat and water soluble vitamins should be given daily, ideally from the commencement of PN in order to maintain standard daily requirements.
- Both fat and water soluble vitamins should be given within the lipid emulsion in order to improve their stability.

### 3.6.2 Iron, minerals and trace elements.

The individual requirements for minerals and trace elements also remain a matter of debate (8). Trace elements are involved in enzymatic activities and immunological reactions, infants are

consequently at risk of trace element deficiency secondary to low body stores at birth and the high demands of rapid growth. (49 50) Parenteral mineral and trace element recommendations are consequently calculated to prevent the development of deficiency syndromes (51) and match in-utero accretion rates (52).

Infants receiving PN for >3 weeks, with minimal or no enteral feeds, may require additional parenteral zinc supplementation (8). Trace element status, including copper should also be monitored monthly in those infants on long term PN (8).

Iron is not routinely provided in neonatal PN and is often not a component of commercially available trace element preparations. Concerns exist regarding iron overload and the role intravenous iron can play in the impairment of immune function and the increase in infection risk secondary to bacterial overgrowth (53). It is therefore preferable for supplemental iron to be given enterally rather than parenterally where tolerated. (8). NICE does not recommend parenteral iron for any infant under 28 days of age (7)

Where a preterm infant receives PN as the sole source of nutrition for >21 days, ESPGHAN recommend that iron status be closely monitored using serum ferritin levels and a regular daily dose of parenteral iron (between 100microgram and 200microgram/kg/day) be considered where indicated. (8).NICE recommend monitoring for iron deficiency and treating as necessary in infants who are 28 days or older (7)
Iron sucrose is the most studied preparation used in children and is recommended for intermittent infusion. (8).

**Recommendations:**

- For **preterm and term infants** intravenous trace elements should be given from the commencement of PN
- Intravenous iron should not be given to any infant under the age of 28 days
- Infants on sole PN who are 28 days or older should be monitored for iron deficiency and treated if necessary
- Infants receiving PN >21 days should be considered for additional supplementation of zinc.
- Trace elements and fat soluble vitamin levels should be monitored monthly in all infants receiving long term PN

## 3.7 Calcium and Phosphorus

In infants the retention of calcium and phosphorus is proportional to growth (54), such that foetal bone mineral accretion rates of 2mmol Ca and 1.52mmol P per 10g newly grown body weight can be achieved if the infant receives adequate quantities of both minerals. (55) Phosphorus is also a component of lean tissue and an important substrate for muscle function. The provision of phosphorus for tissue accretion in the growing body therefore has priority. At times where there is an inadequate supply of phosphorus any available substrate is primarily directed to cellular metabolism, reducing bone mineralisation or even inducing bone demineralisation, (56) therefore, the priority in provision of early or incomplete PN is the provision of sufficient phosphorus in order to avoid severe hypophosphataemia. PN, especially when containing recommended levels of amino acid, should have a molar Ca:P ratio in the PN solution of between 0.75:1 and 1:1 for both preterm and term infants. (7)

**Recommendations**

- For **preterm infants** starting PN within the first 48 hours after birth:
- Give a starting range of 0.8 – 1.0mmol/kg/day Calcium
- Give 1.0mmol/kg/day Phosphate, increasing to 2mmol/kg/day after 48 hours
- For **preterm infants** starting PN more than 48 hours after birth:

- Give a range of 1.5 - 2.0mmol/kg/day Calcium
- Give 2.0mmol/kg/day Phosphate. Careful monitoring of the plasma phosphate concentration is required within the first days of life, with the need for possible higher doses of phosphate to prevent severe hypophosphataemia in preterm infants.
- A calcium to phosphate ratio of 0.75:1 – 1:1 should be used for all neonates receiving PN.

## 4.0 Parenteral nutrition in the critically ill preterm and term neonate

The nutritional management of critically ill neonates varies widely, and there is considerable debate as to the optimal time to commence nutrition support, energy requirements and composition of administered feeds.
The acute metabolic response to critical illness is characterised by an immediate period of depressed metabolism followed by a more prolonged period of increased metabolic activity in the form of catabolism.
In the early phase (6-24hours) glycogen stores are degraded to cover energy needs, whilst protein and fat are concurrently mobilised – protein to provide specific amino acids for gluconeogenesis and synthesis in the liver of acute phase reactants such as CRP, and fat for the provision of free fatty acids and glycerol. This mobilisation of energy through muscle and fat catabolism can result in a temporary cessation of growth, hence the established recommendation to adapt nutritional care in line with the different phases of the metabolic stress response in order to avoid the risk of overfeeding during the early catabolic phase of illness and underfeeding during the late acute and recovery phases. However this proves challenging in clinical practice as ideally nutritional care of the critically ill neonate should be based on true assessment of energy expenditure – a process that is unrealistic in the acute setting.

Studies on current nutritional practices in critically ill preterm and term infants show that they accumulate significant protein and energy deficits over their neonatal course, which can account for as much as 40-45% of the weight of age z-score variation seen during hospital stay (CC 40.49). This is due to prescribed and actually delivered nutrient intakes being below accepted recommendations, with additional compromise to nutrient supply by carbohydrate and lipid intolerance (resulting in hyperglycaemia and lipaemia), by fluid restriction, concomitant medical infusions or lack of adequate access for nutrition support.

In response to a large RCT looking at the early and late provision of nutrition to critically ill children (the PEPaNIC study), PN guidelines from ESPGHAN (8) recommend that clinicians consider "withholding PN, including amino acids for 1 week in critically ill term infants", However a more recent position paper from ESPGHAN that looked more specifically at the nutritional management of the critically ill neonate, conclude that although there is a body of evidence that indicates energy expenditure in critical illness is substantially lower than predicted, there is insufficient data to make any firm recommendations on the optimal timing and composition of nutrition support for critically ill term and preterm infants (20). This view is further supported by a Cochrane review on early versus late PN for critically ill term and late preterm infants, where the authors conclude that "there is insufficient evidence from randomised controlled trials to determine whether early or late commencement of PN affects the outcomes of critically ill term and late preterm infants". (57).

ESPGHAN go on to recommend that for the preterm infant current evidence does not support any significant changes to current guidelines, which in response to the evidence for reduced energy expenditure in critical illness, recommend that critically ill preterm infants should receive nutritional support "started at the minimal amount needed to cover basal metabolic rate and basic macronutrient needs during the early acute phase of the illness"
For the term neonate ESPGHAN recommend not to withhold PN but to commence nutrition support after 48 hours. This should be at the infant's predicted resting energy expenditure and should include micronutrients.

NICE recommend that term infants who are critically ill or who have just had surgery be given PN with energy at the lower end of the starting range, with gradual increase to the intended maintenance intake.(7)

Recommendations:

- For critically ill **preterm infants** give PN in accordance with the East of England guidelines, commencing at a rate of 40kcal/kg/day, increasing gradually to target requirement.
- For critically ill **term infants** give PN after 48 hours, commencing at a rate of 40kcal/kg, increasing gradually to target requirement.

## 5.0 Standardised parenteral nutrition

Individualised PN has previously been seen as the “gold standard” for achieving optimal nutritional intake in neonatal PN. However recent recommendations suggest that a more standardised approach should be adopted as a way of improving quality control and good professional practice in the preparation of PN solutions. NICE in 2020 recommended that when starting neonatal PN a standardised formulation, prepared to nationally agreed quality standards, is to be used, and that a standardised approach be continued unless there is a clear clinical requirement for a more individualised approach (7)This recommendation is further supported by NICE Quality Standards, published in 2022 that state that preterm and term babies who are to receive PN are started on a standardised formulation, and that the use of standard bags improves consistency in nutritional care, reduces variation in practice and reduces the risk of errors that can occur when making up individualised prescribed bags. (58)
Recent years have seen a move towards standardisation of neonatal PN (59) where with careful attention to local workload, formulations and PN prescribing practices the majority of infants can be managed using standardised regimens (60,61). The Paediatric Chief Pharmacists Group state in their 2011 report that the rationalisation and standardisation of PN formulations, where appropriate, has an important part to play in simplifying both the prescribing and compounding processes in PN production.(5) Through removing the need for multiple additions during the compounding process standardisation may be related to a lower risk of error and could apply to 80% of neonatal prescriptions. It may also enable the improvement of early nutrient supply with associated better weight gain and fewer nutritional deficits (62) and allow for the advance preparation of solutions by pharmacies and commercial providers, facilitating end product testing and quality assurance by the provider.
Batch-produced standardised PN bags can be readily available as ward stock, thus allowing initiation of PN immediately after the delivery of a premature infant (63), whilst sourcing commercially prepared standard PN bags may reduce the large costs associated with individualised PN provision (64) and decrease the risk of ordering errors as well as the risk of compounding errors in the hospital pharmacy.
PN is a product with more than 50 ingredients and additives and, as such, is liable to medication errors. The ordering process is time consuming, involves risk and necessitates knowledge and experience (65,66). Development of a standardised PN order form, including age and weight-specific nutrient requirements alongside clinical PN guidelines may help clinicians (especially if inexperienced,) by facilitating PN prescription and decreasing prescribing errors (67)

The inclusion of trace elements in aqueous PN has until recently shortened the shelf life of the bag to approx. 7 days, making management of batch stock control untenable for units with no pharmacy aseptic unit. Work undertaken in 2019 with commercial suppliers has enabled the design and construction of EoE standardised formulations that have 60 – 89 day stability with added trace elements, thereby enabling all units to manage batch stock control of preterm PN bags.

A term concentrated bag has been added to the EOE standard range to accommodate the requirements of cooled and post-surgical term infants who may require reduced volume or longer term PN. At present this formulation is not available off the EOE Tender Framework, however work is ongoing to secure stability data for direct off contract ordering from suppliers. Please contact author for further information if you wish to use this formulation.

**Recommendation:**

- Standardised PN bags are to be used in order to maximise nutrient delivery and to minimise the risk of errors in prescription and compounding.
- The EoE "preterm concentrated" formulation should be used as first line PN to allow for maximum delivery of nutrition within a limited volume (7).
- The decision to use individualised/bespoke PN should only to be made by a senior clinician in conjunction with a neonatal pharmacist and neonatal dietitian.
- Individually tailored PN solutions should only be used when an infant's nutritional requirements cannot be met by the available range of standard PN formulations (i.e. in very sick and metabolically unstable patients such as those with complex disorders associated with fluid and electrolyte imbalance or renal failure.(7)).

## 6.0 Service Design

There is some limited evidence that multidisciplinary team services improve outcomes in newborn babies (7). This alongside acknowledged inadequacies in the provision of neonatal parenteral nutrition (5) has let to recommendations for PN services to be overseen and supported by a MDT with specific expertise in neonatal PN (7 58). Membership of the team should ensure that there is expertise in clinical, prescribing and nutritional core components of PN and comprise at a minimum of a consultant neonatologist or paediatrician with a special interest in neonatology, a neonatal dietitian and a neonatal pharmacist. This support team could be available at either local unit level or within a clinical network with added access to an enhanced MDT for the assessment and support of preterm and term babies with complex nutritional needs.(7 58)

**Recommendations:**

- Neonatal PN services should be supported by a specialist MDT, either locally or at network level.

- The team should comprise, at a minimum of a consultant, a neonatal dietitian and a neonatal pharmacist, with access to a wider team as required for the management of babies with complex needs.

## 7.0 PN associated liver disease

PN associated liver disease (PNALD) is a serious complication of prolonged PN use. Prolonged PN dependence is frequently associated with gastrointestinal conditions that lead to intestinal failure and can be defined as a dependence on PN for some or all nutritional requirements for 28 or more days. Risk factors for PNALD include prematurity, surgical conditions such as gastroschisis, jejunal atresia, NEC which may lead to short gut and/or dysmotility, intestinal failure, intolerance of enteral intake and sepsis.

One factor contributing to the development of PNALD is thought to be the composition of intravenous lipid emulsions. The lipid emulsion most frequently used for neonatal PN in the East of England is based on soya bean oil. Soy based emulsions are rich in omega-6 fatty acids and phytosterols, both of which are known to be inflammatory compounds which may contribute to liver injury. It has been postulated that using an alternative lipid preparation containing higher proportions of omega-3 fatty acids as fish oils can improve and/or reverse liver disease over a 4-6week period (68-71), however the evidence for this remains limited ESPGHAN PN guidance recommend the discontinuation of soya lipid emulsions and the use of composite lipid emulsions containing fish oils as part of a strategy for managing existing PNALD (8) with a further meta-analysis undertaken in 2016 recommending that composite lipid emulsions containing fish oil (eg SMOFLipid) be considered in infants and children with intestinal failure associated liver disease (72). In contrast a recent Cochrane Review concluded that there is currently insufficient evidence to confirm the benefit of using fish oil containing lipid emulsions to improve liver related outcomes for infants with pre-existing liver disease or surgical conditions (46)

Preterm infants on the neonatal unit with significant PN associated liver disease should ideally be discussed with paediatric gastroenterology teams and consideration be given to the possible use of composite emulsions including fish oil, reduction in lipid dose or cycling of lipid, especially in older infants who are partially enterally fed.(73)

**Recommendations:**

- The use of pure fish oil lipid emulsions is not recommended for general use in preterm infants
- Use a composite emulsion containing fish oil as first line lipid in the following infants:
    - Definitive diagnosis of short gut at commencement of PN eg complex gastroschisis where feeds are unlikely to be established within 28 days.
- Consider using SMOFLipid in the following infants:
    - Infants at high risk of needing PN for >28 days.
    - PN dependent >28 days even if liver function tests are normal.
    - Significant liver dysfunction before 28 days on PN conjugated bilirubin >50micromol/litre ultrasound evidence of hepatomegaly, or clinical cholestasis (pale stools, dark urine)

## 8.0 Enteral Nutrition

The provision of nutritionally insignificant volumes of enteral nutrition as trophic feeds have been found to encourage intestinal adaptation and have been linked to enhanced gut motility, decreased incidence of PN-induced cholestasis and bacterial translocation. Trophic feeds should be considered early in infants receiving PN (where clinically indicated) in order to utilise maternal colostrum and stimulate gut trophic hormones.

The maximum volume classed as a “trophic feed” is 1ml/kg/hour or 24ml/kg/day (74) however there is no recognised consensus on method of delivery (75). Individual infants should be assessed daily for tolerance and decisions made with regard to the provision of enteral feeds in line with the East of England Neonatal Network Standardised Feeding Regimen (76.)

**Recommendations:**

- Trophic feeds should be commenced as soon as clinically indicated in the infant receiving parenteral nutrition.
- Decisions regarding enteral feeds should be made in line with the East of England Enteral Feeding guideline.

## 9.0 Monitoring of Parenteral Nutrition

Serious and unexpected biochemical instability as a consequence of PN is rare, but can be potentially fatal. Routine biochemical monitoring against an agreed protocol which takes account of length of time on PN, prematurity, co-morbidities and other administered medicines is therefore crucial (5). It is essential that the individual responsible for reviewing biochemical results and taking appropriate action when abnormal values are observed is clearly identified in each unit (5).
Below is a suggested schedule of monitoring based on NICE and European recommendations for practice (7 / 8). Requirements may differ for individual infants and situations.

| | Starting and increasing PN | Maintenance PN | Comment: |
|---|---|---|---|
| Blood glucose | 1-2 hours after first starting PN | 1-2 hours after each change of PN bag ( 24 or 48 hourly) | Measure more frequently if:<br>• Previous hypo/hyper glycaemia<br>• Dose of IV glucose is changed<br>• Clinical reasons for concern |
| Blood pH | daily | Twice weekly | Measure more frequently if:<br>• Previous levels out of normal range<br>• Clinical reasons for concern |
| Potassium | daily | Twice weekly | Measure more frequently if:<br>• Previous levels out of normal range<br>• IV dose has changed<br>• Clinical reasons for concern |
| Chloride | daily | Twice weekly | Measure more frequently if:<br>• Previous levels out of normal range<br>• IV dose has changed<br>• Clinical reasons for concern |
| Calcium | Daily | Twice weekly | Measure more frequently if:<br>• Previous levels out of normal range<br>• IV dose has changed<br>• Clinical reasons for concern |
| Sodium | daily | Twice weekly | No recommendation |
| Phosphate | daily | Weekly | Measure more frequently if:<br>• If level has been outside normal range<br>• Clinical reason for concern<br>• Preterm infants born <32+0 weeks |
| Urea & Creatinine | Daily | Twice weekly | No recommendation |
| Magnesium | Twice weekly | Twice weekly | No recommendation |
| Iron status | | | Measure ferritin, iron and transferrin saturation if a preterm baby is on PN for >28 days |
| Liver function | weekly | weekly | Measure more frequently if:<br>• Previous levels outside normal range<br>• Clinical reasons for concern |
| Triglycerides | Daily | weekly | Measure more frequently (but not more than 1x day) if:<br>• Level is >3.0 mmol/l<br>• Baby is at risk of hypertriglyceridaemia |

### 9.1 Long term PN

Infants receiving PN long-term, i.e. >3 weeks with minimal or no enteral feeds and those with pre-existing imbalances or reduced excretion of bile or urine as in cholestasis, renal failure or hepatic disease should receive the following additional monitoring on a monthly basis(8):

- trace element status, including copper, manganese, selenium and zinc.
- fat soluble vitamin status (vitamins A, D, E)

### 9.2 Triglyceride monitoring (Tg)

Tolerance of lipid administration can be assessed by measurement of plasma triglyceride concentrations.
However, a normal plasma triglyceride concentration does not necessarily mean optimal oxidation of lipids so it is unclear at what level of triglycerides adverse effects may occur (77).

Hypertriglyceridaemia might occur because of lipogenesis secondary to the provision of too much glucose. Therefore glucose intake should be reviewed and reduced to recommended levels before any amendment is made to lipid infusion rates. Hypertriglyceridaemia may also occur in patients with sepsis.
Preterm infants have relatively limited muscle and fat mass and therefore decreased hydrolytic capacity, as a result they may be at higher risk of raised triglyceride levels than term infants (78). Enteral feeds can contribute to triglyceride levels, consequently ongoing monitoring may not be needed for stable preterm and term infants transitioning from PN to enteral feeds (7).
In a study on early lipid administration to VLBW infants, the occurrence of hypertriglyceridaemia (defined as >3 mmol/L) was not associated with a higher incidence of neonatal morbidities (19) therefore in the absence of other evidence it seems acceptable to consider reducing lipid infusions when concentrations exceed 3.0m mol/L (265 mg/dL) and where glucose provision is known to be within the normal range

Where triglyceride levels are above the defined limits, lowering, not stopping the lipid dosage is recommended. A minimum lipid intake of 0.5g[2.5ml]/kg/day Intralipid or 1.5g[7.5ml]/kg/day SMOFLipid is required to meet essential fatty acid requirement.
If lipid infusion is interrupted consideration should be given to the provision of vitamins. Whereas water soluble vitamins can be added to the aqueous PN there will be no fat soluble vitamin provision until infusion recommences.

**Recommendations:**

- All infants on PN should receive consistent regular monitoring.
- Infants receiving PN long-term, i.e. >3 weeks with minimal or no enteral feeds should receive additional monthly monitoring of trace elements and fat soluble vitamins.
- Triglycerides should be monitored with each increase of IV lipids and weekly after the maximum dose is achieved and tolerated.
- Lipid provision should preferably be reduced, not stopped, when triglyceride levels are above 3.0mmol/L in order to maintain essential fatty acid provision.

# Prescribing and Administration Guideline

## 10.0 Prescribing and Compounding

The decision to initiate PN should be made by a senior clinician (5) following the guidance in Table 1.

The standardised EOE Neonatal Network PN bags with electrolytes and trace elements, should be used as default formulations as the use of standardised nutrient formulations reduces the risk of errors in prescription and compounding of PN (5, 7, 58).

Use of the preterm concentrated formulation will allow for maximum provision of nutrients within limited starting volumes and should therefore be considered as the first line option for preterm PN across the network (7)

Experience and audit shows that 75% of neonatal PN prescribed within the network is completely standard. There will however be occasions when the standard electrolyte provision does not meet an infant's clinical electrolyte requirements (most frequently sodium). NICE recommend that additional supplements, where required, be given using a separate intravenous infusion in order to minimise interference with standard PN bags. (7)

"Fine tuning" of individual electrolyte provision based on detailed calculated mmol/kg requirements is not recommended as practice has shown serum levels remain stable in the majority of infants using the standard provisions.

Fully bespoke or individualised PN should only be used where there is no suitable standardised formulation available to meet unusual nutrient requirements or severe fluid restriction. Care should be taken to ensure the prescription meets published recommended nutrient intakes (4,5). Fully bespoke/individualised PN should only be prescribed with the support of both a neonatal pharmacist and a neonatal dietitian.

Neonatal PN services should be supported by a suitably experienced specialist multidisciplinary team (either local or within a clinical network). (7 58)

The neonatal PN team should include as a minimum, a consultant neonatologist or paediatrician with special interest in neonatology,, a neonatal pharmacist and a neonatal dietitian with experience and expertise in neonatal PN., with further support available from a neonatal nurse, a paediatric a gastroenterologist and an expert in clinical biochemistry.(5, 7 58)

The clinician that decides on the nutrient requirements and the PN formulation should also sign the prescription (5)

PN should ideally be prescribed 48 hourly. Infants with changing electrolyte requirements should, wherever possible be managed with a standard formulation prescribed over 48 hours, supplemented by a separate infusion of electrolytes (7) rather than with a manipulated bag.

The volume of PN prescribed will depend on overall fluid requirements, other infusions (IV medications) and enteral feed volumes. Fluid volume priority should be given to PN in order to maximise nutrient provision, this is more achievable when using the concentrated formulation. Refer to Appendix 2 for PN nutrient composition tables for standard and concentrated bags related to volume per kg/day to ensure volume prescribed satisfies nutritional requirements.

Lipid should not provide more than 40% of non-protein energy requirements therefore when prescribing consideration should be given to the balance of lipid:glucose calorie provision.

Both fat and water soluble vitamins should be given with the lipid emulsion to improve vitamin stability.(47) In units where vitamin and mineral additions are to be made locally the following formulation should be adopted::

| |
|---|
| Intralipid SMOFLipid 20% 37.5ml<br>Vitlipid N Infant 10ml<br>Solivito N (WFI 10ml) 2.5ml<br><br>20ml/kg would then provide:<br>Solivito 1ml/kg<br>Vitlipid N 4ml/kg<br>Lipid 3.4g /kg |

Consideration should be given to other routes of vitamin administration if the lipid emulsion is, for some reason, stopped rather than reduced.(5) Solivito can be added to aqueous PN if necessary but this route should only be used if lipid is not being given.

PN should be prescribed based on birth weight in the first week of life. Thereafter it should be prescribed on the greatest recent weight (birth weight or current weight) as long as there is no significant oedema.

Any change in infusion rate from that on the label of the PN solution must be within the maximal rate of infusion on the label and be clearly documented on the patient's prescription chart.(5)

In chronic or acute severe renal failure trace element preparations should be used with caution along with careful monitoring of trace elements. Such infants may require individually constructed "bespoke" PN (7)

## 11.0 Administration

## 11.1 Central line delivery of PN

Prolonged PN should be given via a central line (8); either a properly sited umbilical venous catheter or peripheral percutaneous central venous line (long-line). Where umbilical venous catheters are used they should not be left in place for more than 14 days (8).

A central line should be used to deliver neonatal PN. (7) It must be inserted according to local/network guidelines with strict adherence to approved aseptic techniques. The line tip position must be confirmed by x-ray (with radio-opaque contrast for long-lines) (79) prior to the infusion of PN. The preferred position for the central line tip should be either the IVC (level of the diaphragm) or SVC (80) (long-line only). Atrial positioning should be avoided due to the risk of atrial perforation (81-83).

Catheter-related blood stream infection remains the most common complication related to central venous access therefore meticulous attention to sterility of the line that is used for PN delivery is vital. Lines used for PN should not be used for blood sampling. Access to the line should be minimised and ideally the line should be used solely for PN, although in the Neonatal Intensive Care setting this is often impractical due to difficulties in venous access and the need to preserve peripheral veins. If other infusions do need to run alongside the PN then compatibility must be confirmed (8).

### 11.2 Peripheral line delivery of PN

Peripheral venous catheters can be used for the routine administration of PN, but are more frequently used in the short term after an assessment has been made to balance the risks of extravasation injury against potential complications associated with obtaining/maintaining central venous access and the nutritional needs of the infant. Peripheral PN should be considered if:

- It would avoid the delay in starting PN beyond the 8 hour preferred window and avoid any interruptions in PN delivery.
- Short term use of PN is anticipated, for example less than 5 days.
- Central line access is impractical.

If PN is administered via a peripheral line then the maximum osmolarity should be limited. There is debate as to the recommended maximum osmolarity for peripheral administration with two studies reporting contradictory results when using PN formulations with osmolar loads >1000mOsm/l (84) or >900mOsm/l (85). NICE felt unable to make any recommendation as to safe levels of PN concentration for peripheral infusion due to the wide range of concentrations used within available studies.(7).whilst both ESPGHAN and ASPEN recommend less than 900mOsm/L(7) The maximum glucose concentration for peripheral infusion is cited as 12.5% which has an osmolarity of 630mOmol/l (8 ,86). PN that is not suitable for peripheral line administration must be clearly labelled: 'to be given by central line only (5).

The EOE Preterm standard and term standard PN bags are suitable for peripheral infusion. The EOE Concentrated PN bags must <u>never</u> be used for peripheral infusion.

### 11.3 Additions to PN

Additions should not be made to standardised PN solutions, either lipid or aqueous, contained in infusion bags and/or syringes. Where unavoidable they must only be made on a PAU and never at ward level. (5 87)

### 11.4 Light protection

In line with European Medicines Agency and Medicines and Healthcare products Regulatory Agency guidance NICE and ESPGHAN both recommend that lipid and aqueous PN solutions should be protected from light. This includes all bags, infusion sets and syringes (7, 8 58). Light exposure increases the products of oxidation in PN which may contribute to increased oxidative stress in preterm infants (88), whereas light protection decreases the accumulation of triglycerides in plasma and may allow for higher rates of lipid infusion and improved nutrition (89). Light protection also helps to prevent light-induced vitamin degradation (52).
Where units are unable to comply with this recommendation this should be added to the Trust's local risk register.

### 11.5 Infusion times

Aqueous PN solutions should be infused over 48 hours in stable neonates where PN has been plumbed in a pharmacy aseptic unit. Lipid should be infused over 24 hours with syringes changed daily. Short term lipid tolerance is maximised when intravenous lipid emulsions are infused continuously at a steady rate. There is little evidence to suggest that a lipid free interval allows lipids to 'clear' from the plasma or improves tolerance through 'hepatic rest' (90), additionally increased line handling associated with interruptions to lipid delivery could also contribute to higher infection risks (91 92)

### 11.6 Out of hours availability of PN

Each unit must make arrangements for pre-prepared PN (both aqueous solutions and lipid emulsions) to be available 24 hours a day (4) to ensure that all preterm infants meeting the criteria can be commenced on PN as early as possible after the decision to give has been made (9)

### 11.7 Use of filters

Adding a terminal filter to PN infusion sets can remove particulate matter, fungi, bacteria and endotoxins, depending on the size of the filter, although it does make PN significantly more expensive. A Cochrane Review of the use of in-line filters in newborns showed no benefits from the use of filters (93) whilst NICE identified that making up PN in an ASU and the use of bags reduces the risk of bacterial contamination. The EOE delivers lipid in syringes rather than bags, which do carry a higher risk of bacterial contamination ,therefore the EOE recommendation is that PN should be delivered via in-line filters; 0.22 micron filters for aqueous PN and 1.2-1.5 micron filters for lipid emulsions.(8)

The EOE recommendation is that PN giving set and filters should be changed every 48 hours for aqueous PN and every 24 hours for lipid.

### 11.8 Checking of PN

PN infusion set up, attachment of the giving set and connection to the patient should be performed using full aseptic non-touch technique (ANTT).

All PN should be checked against prescription and fluid requirements by two registered nurses, one of whom must be qualified in speciality. Both nurses to remain present until PN infusions are

set up in infusion devices and lines are connected to the patient. A final safety check at the point of administration of PN should be performed including checking the labels of PN solutions (aqueous and lipid) against the prescription for:

- Name of patient and hospital number
- Route of administration (central or peripheral)
- Date of infusion
- Rate of infusion
- Expiry
- Doses of all ingredients prescribed
- Appearance of the parenteral nutrition solutions

All nurses that put up PN infusions should be trained in ANTT and IV management and receive appropriate updates.

Training records should be kept for all nurses to demonstrate individual competence.

## 12.0 Weaning of PN

Enteral feeding should be introduced and advanced according to the EOE Enteral Feeding Guideline (76).

Total nutritional provision from the combination of parenteral and enteral nutrition, baby's tolerance of enteral feeds and the balance between nutritional intake and the risk of venous catheter sepsis should be the primary considerations when deciding to wean down parenteral nutrition. When a decision is made to commence weaning of PN both the aqueous and the lipid components should be reduced proportionately to the increase in enteral feeds. The lipid component should also be reduced in proportion to the reduction in the aqueous volume (8) see table.

| Total volume of PN | Reduce lipid (and vitamin) emulsion to the following volumes |
|---|---|
| Less than 130 ml/kg/day | 15 ml/kg/day |
| Less than 100 ml/kg/day | 10 ml/kg/day |
| Less than 70 ml/kg/day | 5 ml/kg/day |
| Less than 50ml/kg/day | Stop lipid infusion |

PN should be continued until at least 120 -150ml/kg/day of enteral feed is tolerated in order to maximise nutrition provision (7). Total fluid volume may be increased above 150ml/kg/day if needed as long as there are no clinical contraindications in order to avoid ordering excessively small PN volumes.

**Recommendations:**

- Consider stopping PN within 24 hours once enteral volumes of 140-150ml/kg/day have been achieved for infants born before 28+0 weeks
- Consider stopping PN within 24 hours once enteral volumes of 120-140ml/kg/day have been achieved for infants born at or after 28+0 weeks.

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# Appendix 1 EAST OF ENGLAND - STANDARD PRETERM

| Nutrient | Bag 1<br><br>Preterm Standard Per 100ml | Bag 2<br>Preterm standard Electrolyte Free<br>Per 100ml | Nutritional provision<br>Per/kg body weight | Recommended provision<br>ESPGHAN 2018<br>Per kg body weight | Recommended provision<br>NICE 2021<br>Per Kg body weight |
|---|---|---|---|---|---|
| **Volume ml** | | | **130ml/kg aqueous plus 20ml/kg lipid. (total 150ml/kg)** | **140-160ml/kg D7+** | **No recommendation** |
| **Energy Kcal/kg** | | | **90-93kcal/kg total energy** | **Min 45-55kcal/kg day 1<br>90-120 kcal/kg total energy** | **40-60Kcal/kg day 1<br><br>75-120Kcal/kg maintenance** |
| **Lipid mlkg** | **20ml/kg** | **20ml/kg** | **20ml/kg [3.4g/kg with Vits] [4g/kg if no Vits]** | **3-4 FO containing after a "few days" ? SMOFLipid** | **1-2g/kg day 1<br><br>3-4g/kg maintenance** |
| **Aminoacid g** | **2.7g AA** | **2.7g AA** | **3.51g AA** | **1.5g day 1<br>2.5-3.5g day 2 onward plus >65NNKcal<br>>3.5g clin trial only** | **1.5-2g/kg day 1<br><br>3-4g/kg maintenance** |
| **Nitrogen g** | **0.39** | **0.39** | **0.50** | | |
| **Carbohydrate g** | **10** | **10** | **13 (10% dextrose)** | **D1 4-8mg/kg/min (5.8-11.5g/kg/day)<br>D2 onward 8-10 (11.5 – 14.4)<br>Min 4(5.8) max 12 (17.3)** | **6-9g/kg day 1<br><br>9-16g/kg maintenance** |
| **Sodium mmol** | **3.06** | **-** | **4** | **D1-2 0-2<br>D3 0-(3-5)<br>D4+ 2-5** | **No recommendation** |
| **Potassium mmol** | **1.9** | **-** | **2.5** | **D1-3 0-3<br>D4+2-3** | **No recommendation** |
| **Chloride mmol** | **3** | **-** | **4** | **D1-3 0-3<br>D4 2-5** | **No recommendation** |
| **Calcium mmol** | **1.3** | **-** | **1.7** | **0.8-2.0 first days of life<br>1.6-3.5 growing** | **0.8-1.0mmol/kg day 1<br>1.5-2.0mmol/kg maintenance** |
| **Phosphate mmol** | **1.53** | **-** | **2.0** | **1.0-2.0 first days of life 1.6-3.5 growing** | **1.0mmol/kg day 1<br>2.0mmol/kg maintenance** |

| | | | | | |
|---|---|---|---|---|---|
| **Ca:P ratio** | | **-** | **0.8:1.0** | **0.8-1.0 initially** | **(0.75:1) to (1.0:1.0)** |
| **Magnesium mmol** | **0.19** | **-** | **0.25** | **0.1-0.2 first days of life 0.2-0.3 growing** | **No recommendation** |
| **Acetate mmol** | **1.5** | **-** | **2** | | **No recommendation** |
| **Peditrace ml** | **0.77** | **-** | | **-** | |

## EAST OF ENGLAND - PRETERM CONCENTRATED

| Nutrient | Bag 3<br><br>Preterm Concentrated Per 100ml | Bag 4 Preterm concentrated Electrolyte Free Per 100ml | Nutritional provision<br><br>Per/kg body weight | Recommended provision ESPGHAN 2018 Per kg body weight | Recommended provision NICE 2021 Per Kg body weight |
|---|---|---|---|---|---|
| **Volume** | | | **100ml/kg aqueous plus 20ml/kg lipid. (total 120ml/kg)** | **140-160ml/kg D7+** | **No recommendation** |
| **Energy Kcal/kg** | | | **90-93kcal/kg total energy** | **Min 45-55kcal/kgday1<br><br>90-120 kcal/kg total energy** | **40-60Kcal/kg day 1<br><br>75-120Kcal/kg maintenance** |
| **Lipid m/kg** | **20ml/kg** | **20ml/kg** | **20ml/kg [3.4g/kg with Vits] [4g/kg if no Vits]** | **3-4 FO containing after a "few days" ? SMOFLipid** | **1-2g/kg day 1<br><br>3-4g/kg maintenance** |
| **Aminoacid g/100ml** | **3.5g AA** | **3.5g AA** | **3.5g AA** | **1.5g day 1 2.5-3.5g day 2 onward plus >65NNKcal >3.5g clin trial only** | **1.5-2g/kg day 1<br><br>3-4g/kg maintenance** |
| **Nitrogen g/100ml** | **0.50** | **0.50** | **0.50** | | |
| **Carbohydrate g/100ml** | **13** | **13** | **13 (13% dextrose)** | **D1 4-8mg/kg/min (5.8-11.5g/kg/day) D2 onward 8-10 (11.5 – 14.4) Min 4(5.8) max 12 (17.3)** | **6-9g/kg day 1<br><br>9-16g/kg maintenance** |
| **Sodium mmol/100ml** | 4.0 | **-** | **4.0** | **D1-2 0-2 D3 0-(3-5) D4+ 2-5** | **No recommendation** |
| **Potassium mmol/100ml** | 2.4 | **-** | **2.4** | **D1-3 0-3 D4+2-3** | **No recommendation** |
| **Chloride mmol/100ml** | | **-** | **3.9** | **D1-3 0-3 D4 2-5** | **No recommendation** |

| | | | | | |
|---|---|---|---|---|---|
| | 3.9 | | | | |
| **Calcium mmol/100ml** | 1.7 | **-** | **1.7** | **0.8-2.0 first days of life 1.6-3.5 growing** | **0.8-1.0mmol/kg day 1 1.5-2.0mmol/kg maintenance** |
| **Phosphate mmol/100ml** | 2.0 | **-** | **2.0** | **1.0-2.0 first days of life 1.6-3.5 growing** | **1.0mmol/kg day 1 2.0mmol/kg maintenance** |
| **Ca:P ratio** | | **-** | **1:1.06** | ***0.8-1.0 initially*** | ***(0.75:1) to (1.0:1.0)*** |
| **Magnesium mmol/100ml** | 0.24 | **-** | **0.24** | ***0.1-0.2 first days of life 0.2-0.3 growing*** | ***No recommendation*** |
| **Acetate mmol/100ml** | 1.9 | **-** | **1.9** | | ***No recommendation*** |
| **Peditrace ml** | 1.0 | **-** | | | |

## EAST OF ENGLAND - TERM STANDARD

| **Nutrient** | **Bag 5 Term Standard Per 100ml** | **Bag 6 Term Standard electrolyte free Per 100ml** | **Nutritional provision Per/kg body weight** | **Recommended intake ESPGHAN 2018 Per kg body weight** | **Recommended provision NICE 2021 Per Kg body weight** |
|---|---|---|---|---|---|
| **volume** | | | **135ml/kg plus 15ml/kg lipid. (total 150ml/kg)** | **140-160(170)** | **No recommendation** |
| **Energy Kcal/kg** | | | **75.8-78.5kcal/kg/day total energy** | **45-50 acute 60-65 stable 75-85 recovery Total energy** | **40-60Kcal/kg day 1 75-120Kcal/kg maintenance** |
| **Lipid ml/kg** | **15ml/kg** | **15ml/kg** | **15ml/kg [3g/kg if no Vits] [2.55g/kg with Vits ]** | | **1-2g/kg day 1 3-4g/kg maintenance** |
| **Aminoacid g** | **1.85** | **1.85** | **2.5** | **1.5-3** | **1.0-2g/kg day 1 2.5-3.0g/kg maintenance** |
| **Nitrogen g** | **0.26** | **0.26** | **0.36** | | |
| **Carbohydrate g** | **9** | **9** | **12.1** | **D1 2.5-5mg/kg/min (3.6-7.2) Target 5-10 (7.2-14.4)** | **6-9g/kg day 1 9-16g/kg maintenance** |

| | | | | | |
|---|---|---|---|---|---|
| | | | | Min2.5(3.6) max12(17.3) | |
| **Sodium mmol** | **2.2** | **-** | **3** | **2-3** | **No recommendation** |
| **Potassium mmol** | **1.9** | **-** | **2.6** | **1-3** | **No recommendation** |
| **Chloride mmol** | **1.9** | **-** | **2.6** | **2-4** | **No recommendation** |
| **Calcium mmol** | **0.7** | **-** | **0.95** | **0.8-1.5** | **0.8-1.0mmol/kg day 1 1.5-2.0mmol/kg maintenance** |
| **Phosphate mmol** | **0.55** | **-** | **0.74 (plus 0.21 from lipid. Total 0.95 1:1)** | **0.7-1.3** | **1.0mmol/kg day 1 2.0mmol/kg maintenance** |
| **Ca:P ratio** | | **-** | **1:1** | | ***(0.75:1) to (1.0:1.0)*** |
| **Magnesium mmol** | **0.15** | **-** | **0.2** | **0.1-0.2** | ***No recommendation*** |
| **Acetate mmol** | | **-** | | | ***No recommendation*** |
| **Peditrace ml** | **0.74** | **-** | | | |

## EAST OF ENGLAND - TERM CONCENTRATED *

| Nutrient | Bag 7 Term concentrated Per 100ml | Bag 8 Term Concentrated electrolyte free Per 100ml | Nutritional provision Per/kg body weight | Recommended intake ESPGHAN 2018 Per kg body weight | Recommended provision NICE 2021 Per Kg body weight |
|---|---|---|---|---|---|
| **volume** | | | **100ml/kg plus 15ml/kg lipid. (total 115ml/kg)** | **140-160(170)** | **No recommendation** |
| **Energy Kcal/kg** | | | **83.4-86.1 kcal/kg/day total energy** | **45-50 acute 60-65 stable 75-85 recovery Total energy** | **40-60Kcal/kg day 1**<br><br>**75-120Kcal/kg maintenance** |
| **Lipid ml/kg** | **15ml/kg** | **15ml/kg** | **15ml/kg [3g/kg if no Vits] [2.55g/kg with Vits ]** | | **1-2g/kg day 1**<br><br>**3-4g/kg maintenance** |
| **Aminoacid g** | **2.5** | **2.5** | **2.5** | **1.5-3** | **1.0-2g/kg day 1**<br><br>**2.5-3.0g/kg maintenance** |
| **Nitrogen g** | **0.36** | **0.36** | **0.36** | | |
| **Carbohydrate g** | **14** | **14** | **14** | **D1 2.5-5mg/kg/min** | **6-9g/kg day 1** |

| | | | | | |
|---|---|---|---|---|---|
| | | | | **(3.6-7.2) Target 5-10 (7.2-14.4) Min2.5(3.6) max12(17.3)** | **9-16g/kg maintenance** |
| **Sodium mmol** | **3** | **-** | **3** | **2-3** | **No recommendation** |
| **Potassium mmol** | **2** | **-** | **2** | **1-3** | **No recommendation** |
| **Chloride mmol** | **2.6** | **-** | **2.6** | **2-4** | **No recommendation** |
| **Calcium mmol** | **0.95** | **-** | **0.95** | **0.8-1.5** | **0.8-1.0mmol/kg day 1 1.5-2.0mmol/kg maintenance** |
| **Phosphate mmol** | **0.74** | **-** | **0.74 (plus 0.21 from lipid. Total 0.97 1:1)** | **0.7-1.3** | **1.0mmol/kg day 1 2.0mmol/kg maintenance** |
| **Ca:P ratio** | | **-** | **1:1** | | ***(0.75:1) to (1.0:1.0)*** |
| **Magnesium mmol** | **0.2** | **-** | **0.2** | **0.1-0.2** | ***No recommendation*** |
| **Acetate mmol** | | **-** | | | ***No recommendation*** |
| **Peditrace ml** | **1.0** | **-** | | | |

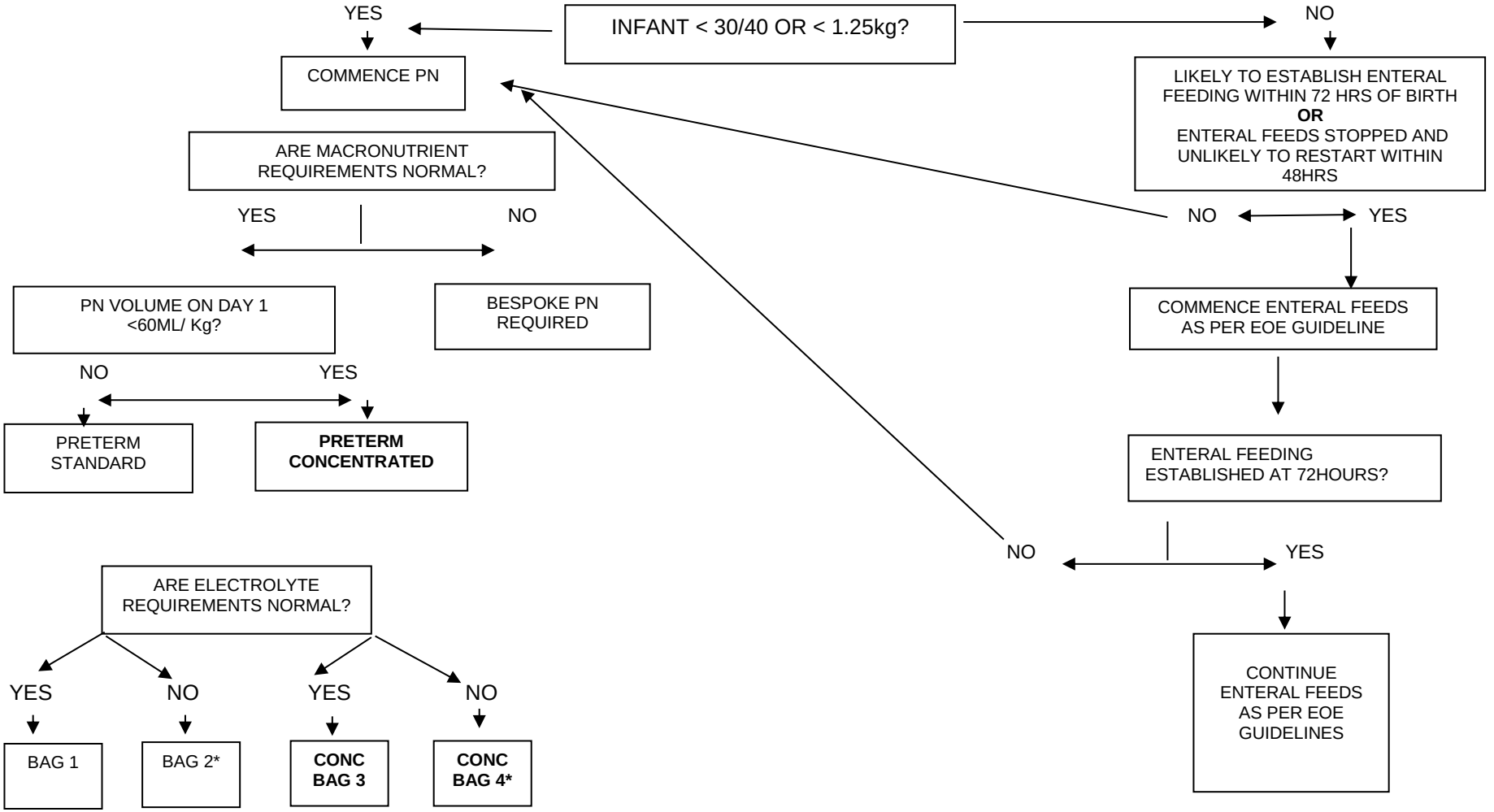
*A term concentrated bag has been added to the EOE standard range to accommodate the requirements of cooled or post-surgical term infants who may require reduced volume or longer term PN. At present this formulation is not available off the EOE Tender Framework, however work is ongoing to secure stability data for direct off contract ordering from suppliers. Please contact author for further information if you wish to use this formulation.

bags - 500ml and 1000ml / Concentrated bags – 400ml and 800ml

Lipid – Intralipid or SMOFLipid prescribed against East of England criteria.

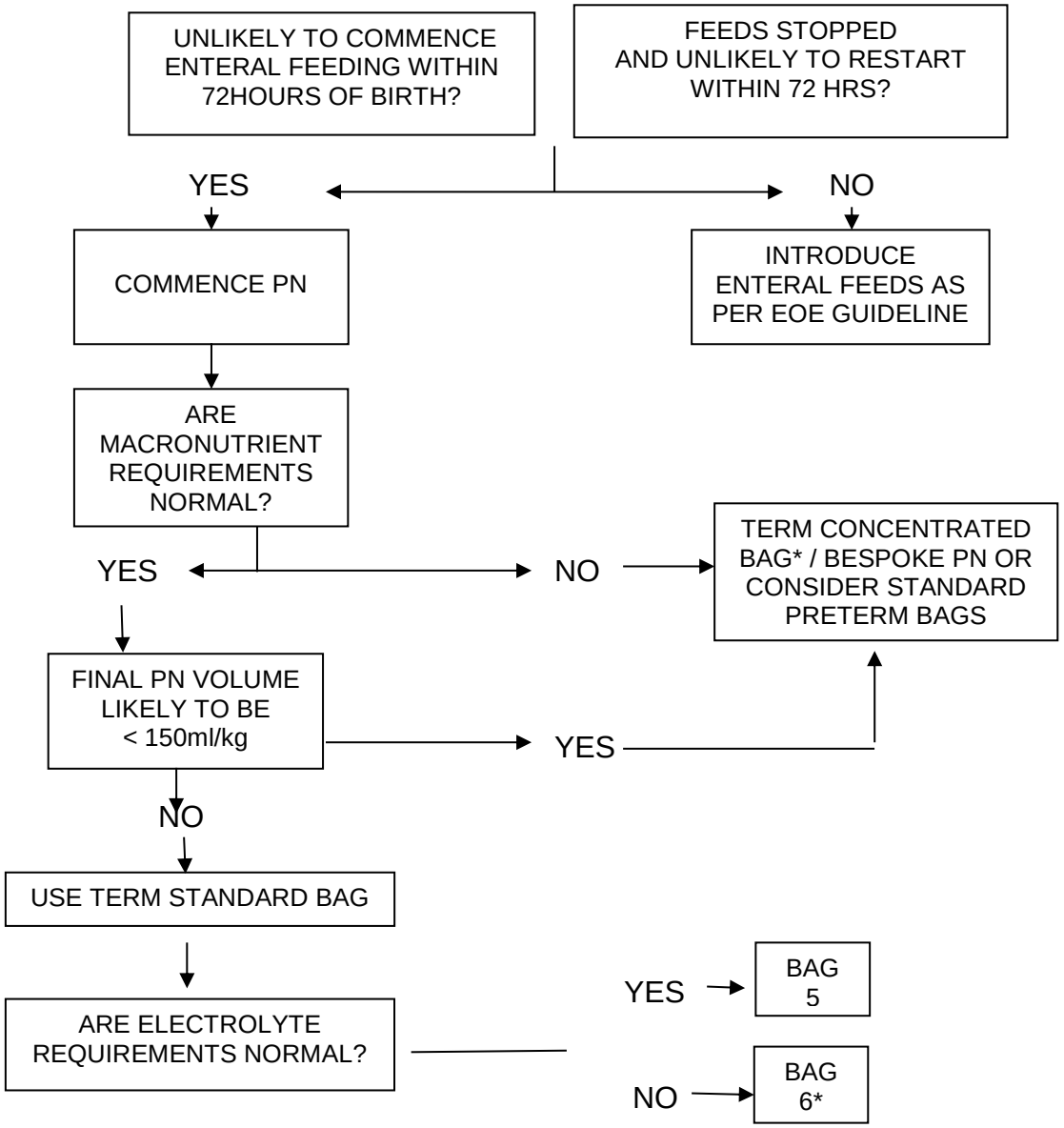
Vitlipid /Solivito as per recommended prescription doses within lipid syringe (see Prescribing Guidelines)

# Appendix 1
## Which bag do I choose for a Preterm infant?




**Preterm Concentrated PN should be the first line choice for all infants in order to maximise nutrient provision**.
'Fine tuning' of electrolytes based on an infant working weight is not recommended. Where required, additional electrolytes should ideally be provided as separate infusions alongside standardised PN bags.
*Electrolyte free bags (bag 2 or 4) should only be used for individual electrolyte prescription when requirements are significantly different from standard provision. They should be prescribed in the "non standard" column of the proforma and ordered either from the local PAU or directly from the supplier for same day delivery

## Which bag do I use for term and near term infants?




'Fine tuning' of electrolytes based on an infant working weight is not recommended.

Where required, additional electrolytes should ideally be provided as separate infusions alongside standardised PN bags.

*Electrolyte free bags (bag 6) should only be used for individual electrolyte prescription when requirements are significantly different from standard provision. They should be prescribed in the "non standard" column of the proforma and ordered either from the local PAU or directly from the supplier for same day delivery.

*A term concentrated bag has been added to the EOE standard range to accommodate the requirements of post-surgical term infants requiring longer term PN. At present this formulation is not available off the EOE Tender Framework, however work is ongoing to secure stability data for direct off contract ordering from suppliers.
Please contact author for further information if you wish to use this formulation.

**Standard Preterm PN (Lipid with vitamins)**

| Total PN Volume ml/kg/day | **50** | **55** | **60** | **70** | **80** | **90** | **100** | **110** | **120** | **130** | **140** | **150** |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Lipid g/kg/day | 0.85 | 0.85 | 0.85 | 0.85 | 1.7 | 1.7 | 1.7 | 2.55 | 2.55 | 2.55 | 2.55 | 3.4 |
| Lipid volume ml/kg/day | 5 | 5 | 5 | 5 | 10 | 10 | 10 | 15 | 15 | 15 | 15 | 20 |
| Aqueous PN volume ml/kg/day | **45** | **50** | **55** | **65** | **70** | **80** | **90** | **95** | **105** | **115** | **125** | **130** |
| Amino acid g/kg/day | 1.21 | 1.35 | 1.48 | 1.75 | 1.88 | 2.15 | 2.43 | 2.56 | 2.8 | 3.1 | 3.37 | 3.5 |
| Nitrogen g/kg/day | 0.17 | 0.19 | 0.21 | 0.25 | 0.27 | 0.31 | 0.35 | 0.37 | 0.4 | 0.44 | 0.48 | 0.5 |
| Carbohydrate g/kg/day | 4.5 | 5.0 | 5.5 | 6.5 | 7.0 | 8.0 | 9.0 | 9.5 | 10.5 | 11.5 | 12.5 | 13.0 |
| Non Nitrogen Energy kcal/kg/day | 27 | 29 | 31 | 35 | 45 | 49 | 53 | 64 | 68 | 72 | 76 | 86 |
| NNEnergy: nitrogen ratio kcal/g | 158 | 152 | 147 | 140 | 167 | 158 | 151 | 173 | 170 | 163 | 158 | 172 |
| NNEnergy:amino acid ratio kcal/g | 22 | 21 | 21 | 20 | 24 | 23 | 22 | 25 | 25 | 23 | 22.5 | 24.5 |
| Lipid calories kcal/kg/day | 8.6 | 8.6 | 8.6 | 8.6 | 17.2 | 17.2 | 17.2 | 25.8 | 25.8 | 25.8 | 25.8 | 34 |
| Lipid/ Non Nitrogen Energy % | 32% | 30% | 28% | 25% | 38% | 35% | 32% | 40% | 38% | 36% | 34% | 39.5% |
| Sodium mmol/kg/day | 1.4 | 1.5 | 1.7 | 2.0 | 2.1 | 2.4 | 2.7 | 2.9 | 3.2 | 3.5 | 3.8 | 3.9 |
| Potassium mmol/kg/day | 0.9 | 1.0 | 1.0 | 1.2 | 1.3 | 1.5 | 1.7 | 1.8 | 2.0 | 2.2 | 2.4 | 2.5 |
| Chloride mmol/kg/day | 1.4 | 1.5 | 1.7 | 2.0 | 2.1 | 2.4 | 2.7 | 2.9 | 3.2 | 3.5 | 3.8 | 3.9 |
| Calcium mmol/kg/day | 0.58 | 0.65 | 0.72 | 0.84 | 0.91 | 1.04 | 1.17 | 1.24 | 1.37 | 1.49 | 1.63 | 1.69 |
| Phosphate mmol/kg/day | 0.69 | 0.76 | 0.84 | 0.99 | 1.07 | 1.27 | 1.38 | 1.45 | 1.6 | 1.76 | 1.91 | 1.98 |
| Ca:P ratio [aqueous] | 0.84:1. | 0.85:1 | 0.86:1 | 0.85:1 | 0.85:1 | 0.85:1 | 0.84:1 | 0.85:1 | 0.85:1 | 0.84:1 | 0.78:1 | 0.85:1 |
| Phosphate from lipd mmol/kg/day | 0.07 | 0.07 | 0.07 | 0.07 | 0.14 | 0.14 | 0.14 | 0.21 | 0.21 | 0.21 | 0.21 | 0.28 |
| Total phosphate mmol/kg/day | 0.76 | 0.83 | 0.91 | 1.06 | 1.21 | 1.41 | 1.52 | 1.67 | 1.81 | 1.99 | 2.12 | 2.26 |
| Magnesium mmol/kg/day | 0.09 | 0.10 | 0.10 | 0.12 | 0.13 | 0.15 | 0.17 | 0.18 | 0.20 | 0.22 | 0.24 | 0.25 |
| Acetate mmol/kg/day | 0.7 | 0.8 | 0.8 | 1.0 | 1.1 | 1.2 | 1.4 | 1.4 | 1.6 | 1.7 | 1.9 | 2.0 |

## Standard Preterm PN (Lipid without vitamins)

| **Total PN Volume ml/kg/day** | **50** | **55** | **60** | **70** | **80** | **90** | **100** | **110** | **120** | **130** | **140** | **150** |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Lipid g/kg/day | 1 | 1 | 1 | 1 | 2 | 2 | 2 | 2 | 3 | 3 | 3 | 4 |
| Lipid volume ml/kg/day | 5 | 5 | 5 | 5 | 10 | 10 | 10 | 10 | 15 | 15 | 15 | 20 |
| **Aqueous PN volume ml/kg/day** | **45** | **50** | **55** | **65** | **70** | **80** | **90** | **100** | **105** | **115** | **125** | **130** |
| Amino acid g/kg/day | 1.21 | 1.35 | 1.48 | 1.75 | 1.88 | 2.15 | 2.43 | 2.56 | 2.8 | 3.1 | 3.37 | 3.5 |
| Nitrogen g/kg/day | 0.17 | 0.19 | 0.21 | 0.25 | 0.27 | 0.31 | 0.35 | 0.37 | 0.4 | 0.44 | 0.48 | 0.5 |
| Carbohydrate g/kg/day | 4.5 | 5.0 | 5.5 | 6.5 | 7.0 | 8.0 | 9.0 | 9.5 | 10.5 | 11.5 | 12.5 | 13.0 |
| Non Nitrogen Energy kcal/kg/day | 28 | 30 | 32 | 36 | 48 | 52 | 56 | 67 | 71 | 75 | 79 | 90 |
| NNEnergy: nitrogen ratio kcal/g | 164 | 158 | 152 | 144 | 177 | 168 | 160 | 181 | 177 | 170 | 164 | 180 |
| NNEnergy:amino acid ratio kcal/g | 23 | 22 | 21.6 | 20.6 | 25.5 | 24 | 23 | 25 | 26 | 24 | 23 | 25.7 |
| Lipid calories kcal/kg/day | 10 | 10 | 10 | 10 | 20 | 20 | 20 | 20 | 30 | 30 | 30 | 40 |
| Lipid/ Non Nitrogen Energy % | 36% | 33% | 31% | 27% | 41% | 38% | 36% | 30% | 42% | 40% | 38% | 44% |
| Sodium mmol/kg/day | 1.4 | 1.5 | 1.7 | 2.0 | 2.1 | 2.4 | 2.7 | 3.0 | 3.2 | 3.5 | 3.8 | 3.9 |
| Potassium mmol/kg/day | 0.9 | 1.0 | 1.0 | 1.2 | 1.3 | 1.5 | 1.7 | 1.9 | 2.0 | 2.2 | 2.4 | 2.5 |
| Chloride mmol/kg/day | 1.4 | 1.5 | 1.7 | 2.0 | 2.1 | 2.4 | 2.7 | 3.0 | 3.2 | 3.5 | 3.8 | 3.9 |
| Calcium mmol/kg/day | 0.58 | 0.65 | 0.72 | 0.84 | 0.91 | 1.04 | 1.17 | 1.24 | 1.37 | 1.49 | 1.63 | 1.69 |
| Phosphate mmol/kg/day | 0.69 | 0.76 | 0.84 | 0.99 | 1.07 | 1.27 | 1.38 | 1.45 | 1.6 | 1.76 | 1.91 | 1.98 |
| Ca:P ratio [aqueous] | 0.84:1. | 0.85:1 | 0.86:1 | 0.85:1 | 0.85:1 | 0.85:1 | 0.84:1 | 0.85:1 | 0.85:1 | 0.84:1 | 0.78:1 | 0.85:1 |
| Phospahte from lipid mmol/kg/day | 0.08 | 0.08 | 0.08 | 0.08 | 0.15 | 0.15 | 0.15 | 0.15 | 0.23 | 0.23 | 0.23 | 0.30 |
| Total phosphate mmol/kg/day | 0.77 | 0.84 | 0.92 | 1.07 | 1.22 | 1.37 | 1.53 | 1.68 | 1.83 | 1.99 | 2.14 | 2.28 |
| Magnesium mmol/kg/day | 0.09 | 0.10 | 0.10 | 0.12 | 0.13 | 0.15 | 0.17 | 0.19 | 0.20 | 0.22 | 0.24 | 0.25 |
| Acetate mmol/kg/day | 0.7 | 0.8 | 0.8 | 1.0 | 1.1 | 1.2 | 1.4 | 1.5 | 1.6 | 1.7 | 1.9 | 2.0 |

**Preterm concentrated Lipid with vitamins**

| **Total PN Volume ml/kg/day** | **50** | **55** | **60** | **70** | **80** | **90** | **100** | **110** | **120** |
|---|---|---|---|---|---|---|---|---|---|
| Lipid g/kg/day | 0.85 | 0.85 | 1.7 | 1.7 | 1.7 | 1.7 | 2.5 | 2.5 | 3.4 |
| Lipid volume ml/kg/day | 5 | 5 | 10 | 10 | 10 | 10 | 15 | 15 | 20 |
| **Aqueous PN volume ml/kg/day** | **45** | **50** | **50** | **60** | **70** | **80** | **85** | **95** | **100** |
| Amino acid g/kg/day | 1.57 | 1.75 | 1.75 | 2.1 | 2.45 | 2.8 | 2.97 | 3.32 | 3.5 |
| Nitrogen g/kg/day | 0.23 | 0.25 | 0.25 | 0.3 | 0.35 | 0.4 | 0.45 | 0.48 | 0.5 |
| Carbohydrate g/kg/day | 5.9 | 6.5 | 6.5 | 7.8 | 9.1 | 10.4 | 11.1 | 12.4 | 13.0 |
| Non Nitrogen Energy kcal/kg/day | 32. | 35 | 43 | 48 | 54 | 59 | 70 | 75 | 86 |
| NNEnergy: nitrogen ratio kcal/g | 139 | 140 | 172 | 160 | 154 | 147 | 156 | 156 | 172 |
| NNEnergy:amino acid ratio kcal/g | 20.3 | 20 | 24.5 | 23 | 22 | 21 | 23.5 | 22.5 | 25 |
| Lipid calories kcal/kg/day | 8.6 | 8.6 | 17.2 | 17.2 | 17.2 | 17.2 | 25.8 | 25.8 | 34 |
| Lipid/ Non Nitrogen Energy % | 27% | 25% | 40% | 36% | 32% | 29% | 37% | 34% | 40% |
| Sodium mmol/kg/day | 1.8 | 2.0 | 2.0 | 2.4 | 2.8 | 3.2 | 3.4 | 3.8 | 4.0 |
| Potassium mmol/kg/day | 1.1 | 1.3 | 1.3 | 1.5 | 1.8 | 2.0 | 2.1 | 2.4 | 2.5 |
| Chloride mmol/kg/day | 1.8 | 2.0 | 2.0 | 2.4 | 2.8 | 3.2 | 3.4 | 3.8 | 4.0 |
| Calcium mmol/kg/day | 0.77 | 0.85 | 0.85 | 1.02 | 1.19 | 1.36 | 1.45 | 1.61 | 1.7 |
| Phosphate mmol/kg/day | 0.9 | 1.0 | 1.0 | 1.2 | 1.4 | 1.6 | 1.7 | 1.9 | 2.0 |
| Ca:P ratio [aqueous] | 0.85:1 | 0.85:1 | 0.85:1 | 0.85:1 | 0.85:1 | 0.85:1 | 0.85:1 | 0.85:1 | 0.85:1 |
| Phosphate from lipid mmol/kg/day | 0.07 | 0.07 | 0.14 | 0.14 | 0.14 | 0.14 | 0.21 | 0.21 | 0.28 |
| Total phosphate mmol/kg/day | 0.97 | 1.07 | 1.14 | 1.34 | 1.54 | 1.74 | 1.91 | 2.11 | .2.28 |
| Magnesium mmol/kg/day | 0.11 | 0.13 | 0.13 | 0.15 | 0.18 | 0.20 | 0.21 | 0.24 | 0.25 |
| Acetate mmol/kg/day | 0.9 | 1.0 | 1.0 | 1.2 | 1.4 | 1.6 | 1.7 | 1.9 | 2 |

## Preterm concentrated PN (Lipid without vitamins)

| **Total PN Volume ml/kg/day** | **50** | **55** | **60** | **70** | **80** | **90** | **100** | **110** | **120** |
|---|---|---|---|---|---|---|---|---|---|
| Lipid g/kg/day | 1 | 1 | 2 | 2 | 2 | 2 | 3 | 3 | 4 |
| Lipid volume ml/kg/day | 5 | 5 | 10 | 10 | 10 | 10 | 15 | 15 | 20 |
| **Aqueous PN volume ml/kg/day** | **45** | **50** | **50** | **60** | **70** | **80** | **85** | **95** | **100** |
| Amino acid g/kg/day | 1.57 | 1.75 | 1.75 | 2.1 | 2.45 | 2.8 | 2.97 | 3.32 | 3.5 |
| Nitrogen g/kg/day | 0.23 | 0.25 | 0.25 | 0.3 | 0.35 | 0.4 | 0.45 | 0.48 | 0.5 |
| Carbohydrate g/kg/day | 5.9 | 6.5 | 6.5 | 7.8 | 9.1 | 10.4 | 11.1 | 12.4 | 13.0 |
| Non Nitrogen Energy kcal/kg/day | 33.6 | 36 | 46 | 51 | 56 | 61.6 | 74 | 79.6 | 92 |
| NNEnergy: nitrogen ratio kcal/g | 146 | 144 | 184 | 170 | 160 | 154 | 172 | 166 | 184 |
| NNEnergy:amino acid ratio kcal/g | 21 | 20 | 26 | 24 | 23 | 22 | 25 | 24 | 26 |
| Lipid calories kcal/kg/day | 10 | 10 | 20 | 20 | 20 | 20 | 30 | 30 | 40 |
| Lipid/ Non Nitrogen Energy % | 28% | 26% | 41% | 36% | 33% | 30% | 38% | 35% | 41% |
| Sodium mmol/kg/day | 1.8 | 2.0 | 2.0 | 2.4 | 2.8 | 3.2 | 3.4 | 3.8 | 4.0 |
| Potassium mmol/kg/day | 1.1 | 1.3 | 1.3 | 1.5 | 1.8 | 2.0 | 2.1 | 2.4 | 2.5 |
| Chloride mmol/kg/day | 1.8 | 2.0 | 2.0 | 2.4 | 2.8 | 3.2 | 3.4 | 3.8 | 4.0 |
| Calcium mmol/kg/day | 0.77 | 0.85 | 0.85 | 1.02 | 1.19 | 1.36 | 1.45 | 1.61 | 1.7 |
| Phosphate mmol/kg/day | 0.9 | 1.0 | 1.0 | 1.2 | 1.4 | 1.6 | 1.7 | 1.9 | 2.0 |
| Ca:P ratio [aqueous] | 0.85:1 | 0.85:1 | 0.85:1 | 0.85:1 | 0.85:1 | 0.85:1 | 0.85:1 | 0.85:1 | 0.85:1 |
| Phosphate from lipid mmol/kg/day | 0.08 | 0.08 | 0.15 | 0.15 | 0.15 | 0.15 | 0.23 | 0.23 | 0.30 |
| Total phosphate mmol/kg/day | 0.98 | 1.08 | 1.15 | 1.35 | 1.55 | 1.75 | 1.93 | 2.13 | 2.3 |
| Magnesium mmol/kg/day | 0.11 | 0.13 | 0.13 | 0.15 | 0.18 | 0.20 | 0.21 | 0.24 | 0.25 |
| Acetate mmol/kg/day | 0.9 | 1.0 | 1.0 | 1.2 | 1.4 | 1.6 | 1.7 | 1.9 | 2 |

**Standard Term PN (Lipid without vitamins)**

| **Total PN Volume ml/kg/day** | **50** | **55** | **60** | **70** | **80** | **90** | **100** | **110** | **120** | **130** | **140** | **150** |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Lipid g/kg/day | 1 | 1 | 1 | 1 | 2 | 2 | 2 | 2 | 3 | 3 | 3 | 3 |
| Lipid volume ml/kg/day | 5 | 5 | 5 | 5 | 10 | 10 | 10 | 10 | 15 | 15 | 15 | 15 |
| **Aqueous PN volume ml/kg/day** | **45** | **50** | **55** | **65** | **70** | **80** | **90** | **100** | **105** | **115** | **125** | **135** |
| Amino acid g/kg/day | 0.83 | 0.9 | 1.0 | 1.2 | 1.3 | 1.48 | 1.67 | 1.85 | 1.94 | 2.13 | 2.31 | 2.5 |
| Nitrogen g/kg/day | 0.12 | 0.13 | 0.15 | 0.17 | 0.19 | 0.21 | 0.24 | 0.26 | 0.28 | 0.31 | 0.33 | 0.36 |
| Carbohydrate g/kg/day | 4.0 | 4.5 | 4.9 | 5.8 | 6.3 | 7.2 | 8.1 | 9.0 | 9.4 | 10.3 | 11.2 | 12.1 |
| NNEnergy kcal/kg/day | 26 | 28 | 29.6 | 33.2 | 45.2 | 48.5 | 52.4 | 56 | 67.6 | 71.2 | 74.8 | 78.4 |
| NNEnergy: nitrogen ratio kcal/g | 216 | 215 | 197 | 195 | 237 | 231 | 218 | 215 | 241 | 229 | 226 | 217 |
| NNEnergy:amino acid ratio kcal/g | 31 | 31 | 29.6 | 27.6 | 34.7 | 32.7 | 31.3 | 30 | 35 | 33.4 | 32.4 | 31.4 |
| Lipid calories kcal/kg/day | 10 | 10 | 10 | 10 | 20 | 20 | 20 | 20 | 30 | 30 | 30 | 30 |
| Lipid/ Non Protein Energy % | 38% | 36% | 34% | 30% | 44% | 41% | 38% | 36% | 44% | 42% | 40% | 38% |
| Sodium mmol/kg/day | 1.0 | 1.1 | 1.2 | 1.4 | 1.5 | 1.8 | 2.0 | 2.2 | 2.3 | 2.5 | 2.8 | 3.0 |
| Potassium mmol/kg/day | 0.9 | 1.0 | 1.0 | 1.2 | 1.3 | 1.5 | 1.7 | 1.9 | 2.0 | 2.2 | 2.4 | 2.6 |
| Chloride mmol/kg/day | 0.9 | 1.0 | 1.0 | 1.2 | 1.3 | 1.5 | 1.7 | 1.9 | 2.0 | 2.2 | 2.4 | 2.6 |
| Calcium mmol/kg/day | 0.32 | 0.35 | 0.39 | 0.46 | 0.49 | 0.56 | 0.63 | 0.7 | 0.74 | 0.81 | 0.88 | 0.95 |
| Phosphate mmol/kg/day | 0.25 | 0.27 | 0.3 | 0.36 | 0.38 | 0.44 | 0.49 | 0.55 | 0.58 | 0.63 | 0.69 | 0.74 |
| Ca:P ratio [aqueous phase] | 1.3:1 | 1.3:1 | 1.3:1 | 1.3:1 | 1.3:1 | 1.3:1 | 1.3:1 | 1.3:1 | 1.3:1 | 1.3:1 | 1.3:1 | 1.3:1 |
| Phospahte from lipd mmol/kg/day | 0.08 | 0.08 | 0.08 | 0.08 | 0.15 | 0.15 | 0.15 | 0.15 | 0.23 | 0.23 | 0.23 | 0.23 |
| Total phosphate mmol/kg/day | 0.2 | 0.2 | 0.2 | 0.2 | 0.3 | 0.3 | 0.3 | 0.4 | 0.4 | 0.5 | 0.5 | 0.5 |
| Magnesium mmol/kg/day | 0.07 | 0.08 | 0.08 | 0.10 | 0.11 | 0.12 | 0.14 | 0.15 | 0.16 | 0.17 | 0.19 | 0.20 |
| Acetate mmol/kg/day | | | | | | | | | | | | |

**Standard Term PN (Lipid with Vitamins)**

| **Total PN Volume ml/kg/day** | **50** | **55** | **60** | **70** | **80** | **90** | **100** | **110** | **120** | **130** | **140** | **150** |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Lipid g/kg/day | 0.85 | 0.85 | 0.85 | 0.85 | 1.7 | 1.7 | 1.7 | 1.7 | 2.55 | 2.55 | 2.55 | 2.55 |
| Lipid volume ml/kg/day | 5 | 5 | 5 | 5 | 10 | 10 | 10 | 10 | 15 | 15 | 15 | 15 |
| **Aqueous PN volume ml/kg/day** | **45** | **50** | **55** | **65** | **70** | **80** | **90** | **100** | **105** | **115** | **125** | **135** |
| Amino acid g/kg/day | 0.83 | 0.9 | 1.0 | 1.2 | 1.3 | 1.48 | 1.67 | 1.85 | 1.94 | 2.13 | 2.31 | 2.5 |
| Nitrogen g/kg/day | 0.12 | 0.13 | 0.15 | 0.17 | 0.19 | 0.21 | 0.24 | 0.26 | 0.28 | 0.31 | 0.33 | 0.36 |
| Carbohydrate g/kg/day | 4.0 | 4.5 | 4.9 | 5.8 | 6.3 | 7.2 | 8.1 | 9.0 | 9.4 | 10.3 | 11.2 | 12.1 |
| NNEnergy kcal/kg/day | 25 | 26 | 28 | 32 | 42 | 46 | 50 | 53 | 63 | 67 | 71 | 75 |
| NNEnergy: nitrogen ratio kcal/g | 208 | 200 | 186 | 188 | 219 | 222 | 208 | 204 | 225 | 216 | 215 | 208 |
| NNEnergy:amino acid ratio kcal/g | 30 | 29 | 28 | 26.6 | 32 | 31 | 30 | 28.6 | 32 | 31 | 31 | 30 |
| Lipid calories kcal/kg/day | 8.6 | 8.6 | 8.6 | 8.6 | 17.2 | 17.2 | 17.2 | 7.28 | 25.8 | 25.8 | 25.8 | 25.8 |
| Lipid/ Non Protein Energy % | 34% | 33% | 31% | 27% | 41% | 37% | 34% | 32% | 41% | 38% | 36% | 34% |
| Sodium mmol/kg/day | 1.0 | 1.1 | 1.2 | 1.4 | 1.5 | 1.8 | 2.0 | 2.2 | 2.3 | 2.5 | 2.8 | 3.0 |
| Potassium mmol/kg/day | 0.9 | 1.0 | 1.0 | 1.2 | 1.3 | 1.5 | 1.7 | 1.9 | 2.0 | 2.2 | 2.4 | 2.6 |
| Chloride mmol/kg/day | 0.9 | 1.0 | 1.0 | 1.2 | 1.3 | 1.5 | 1.7 | 1.9 | 2.0 | 2.2 | 2.4 | 2.6 |
| Calcium mmol/kg/day | 0.32 | 0.35 | 0.39 | 0.46 | 0.49 | 0.56 | 0.63 | 0.7 | 0.74 | 0.81 | 0.88 | 0.95 |
| Phosphate mmol/kg/day | 0.25 | 0.27 | 0.3 | 0.36 | 0.38 | 0.44 | 0.49 | 0.55 | 0.58 | 0.63 | 0.69 | 0.74 |
| Ca:P ratio [aqueous phase] | 1.3:1 | 1.3:1 | 1.3:1 | 1.3:1 | 1.3:1 | 1.3:1 | 1.3:1 | 1.3:1 | 1.3:1 | 1.3:1 | 1.3:1 | 1.3:1 |
| Phosphate from lipid mmol/kg/day | 0.07 | 0.07 | 0.07 | 0.07 | 0.14 | 0.14 | 0.14 | 0.14 | 0.21 | 0.21 | 0.21 | 0.21 |
| Total phosphate mmol/kg/day | 0.32 | 0.34 | 0.37 | 0.44 | 0.52 | 0.58 | 0.63 | 0.64 | 0.79 | 0.84 | 0.9 | 0.95 |
| Magnesium mmol/kg/day | 0.07 | 0.08 | 0.08 | 0.10 | 0.11 | 0.12 | 0.14 | 0.15 | 0.16 | 0.17 | 0.19 | 0.20 |