



# Neonatal parenteral nutrition

NICE guideline

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## Your responsibility

The recommendations in this guideline represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, professionals and practitioners are expected to take this guideline fully into account, alongside the individual needs, preferences and values of their patients or the people using their service. It is not mandatory to apply the recommendations, and the guideline does not override the responsibility to make decisions appropriate to the circumstances of the individual, in consultation with them and their families and carers or guardian.

All problems (adverse events) related to a medicine or medical device used for treatment or in a procedure should be reported to the Medicines and Healthcare products Regulatory Agency using the [Yellow Card Scheme](#).

Local commissioners and providers of healthcare have a responsibility to enable the guideline to be applied when individual professionals and people using services wish to use it. They should do so in the context of local and national priorities for funding and developing services, and in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities. Nothing in this guideline should be interpreted in a way that would be inconsistent with complying with those duties.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should [assess and reduce the environmental impact of implementing NICE recommendations](#) wherever possible.

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This guideline is the basis of QS205.

## Overview

This guideline covers parenteral nutrition (intravenous feeding) for babies born preterm, up to 28 days after their due birth date and babies born at term, up to 28 days after their birth. Parenteral nutrition is often needed by preterm babies, critically ill babies, and babies who need surgery.

The recommendations in this guideline were developed before the COVID-19 pandemic.

## Who is it for?

- Healthcare professionals who care for newborn babies
- Commissioners and providers of neonatal care services
- Parents and carers of babies who need parenteral nutrition

# Recommendations

Parents and carers have the right to be involved in planning and making decisions about their baby's health and care, and to be given information and support to enable them to do this, as set out in the NHS constitution and summarised in [making decisions about your care](#).

[Making decisions using NICE guidelines](#) explains how we use words to show the strength (or certainty) of our recommendations, and has information about prescribing medicines (including off label use), professional guidelines, standards and laws (including on consent and mental capacity), and safeguarding.

## 1.1 Indications for, and timing of, neonatal parenteral nutrition

### Indications for starting neonatal parenteral nutrition

- 1.1.1 For [preterm](#) babies born before 31+0 weeks, start neonatal parenteral nutrition.
- 1.1.2 For preterm babies born at or after 31+0 weeks, start parenteral nutrition if sufficient progress is not made with enteral feeding in the first 72 hours after birth.
- 1.1.3 Start parenteral nutrition for preterm and term babies who are unlikely to establish sufficient enteral feeding, for example, babies with:
  - a congenital gut disorder
  - a critical illness such as sepsis.

## Indications for starting neonatal parenteral nutrition if enteral feeds are stopped

- 1.1.4 For preterm babies on enteral feeds, start parenteral nutrition if:
- enteral feeds have to be stopped and it is unlikely they will be restarted within 48 hours
  - enteral feeds have been stopped for more than 24 hours and there is unlikely to be sufficient progress with enteral feeding within a further 48 hours.
- 1.1.5 For term babies on enteral feeds, start parenteral nutrition if:
- enteral feeds have to be stopped and it is unlikely they will be restarted within 72 hours
  - enteral feeds have been stopped for more than 48 hours and there is unlikely to be sufficient progress with enteral feeding within a further 48 hours.

## Timing of starting neonatal parenteral nutrition

- 1.1.6 When a preterm or term baby meets the indications for parenteral nutrition, start it as soon as possible, and within 8 hours at the latest.

For a short explanation of why the committee made these recommendations and how they might affect practice, see the [rationale and impact section on indications for, and timing of, neonatal parenteral nutrition](#).

Full details of the evidence and the committee's discussion are in [evidence review A1: predictors of enteral feeding success](#) and [evidence review A2: optimal timeframe to start parenteral nutrition](#).

## 1.2 Administration of neonatal parenteral nutrition

### Venous access

- 1.2.1 Use a central venous catheter to give neonatal parenteral nutrition. Only consider using peripheral venous access to give neonatal parenteral nutrition if:
- it would avoid a delay in starting parenteral nutrition
  - short-term use of peripheral venous access is anticipated, for example, less than 5 days
  - it would avoid interruptions in giving parenteral nutrition
  - central venous access is impractical.
- 1.2.2 Only consider surgical insertion of a central venous catheter if:
- non-surgical insertion is not possible
  - long-term parenteral nutrition is anticipated, for example, in short bowel syndrome.

For a short explanation of why the committee made these recommendations and how they might affect practice, see the [rationale and impact section on administration of neonatal parenteral nutrition](#).

Full details of the evidence and the committee's discussion are in [evidence review B: venous access](#) and [evidence review J: general principles](#).

### Protection from light

- 1.2.3 Protect the bags, syringes and infusion sets of both aqueous and lipid parenteral nutrition solutions from light.



For a short explanation of why the committee made this recommendation and how it might affect practice, see the [rationale and impact section on administration of neonatal parenteral nutrition](#).

Full details of the evidence and the committee's discussion are in [evidence review B: venous access](#) and [evidence review J: general principles](#).

## 1.3 Energy needs of babies on neonatal parenteral nutrition

1.3.1 For preterm and term babies who need total neonatal parenteral nutrition, deliver energy as follows:

- If starting parenteral nutrition in the first 4 days after birth:
  - give a starting range of 40 to 60 kcal/kg/day
  - gradually increase (for example, over 4 days) to a maintenance range of 75 to 120 kcal/kg/day.
- If starting parenteral nutrition more than 4 days after birth:
  - give a range of 75 to 120 kcal/kg/day.

1.3.2 For preterm and term babies who are on enteral feeds in addition to neonatal parenteral nutrition, reduce the amount of energy that is given parenterally as enteral feeds increase.

### Term babies who are critically ill or have just had surgery

1.3.3 For term babies who are critically ill or have just had surgery, consider giving parenteral energy at the lower end of the starting range in recommendation 1.3.1, and gradually increase to the intended maintenance intake.

For a short explanation of why the committee made these recommendations and how they might affect practice, see the [rationale and impact section on energy needs of babies on neonatal parenteral nutrition](#).

Full details of the evidence and the committee's discussion are in [evidence review C: energy needs](#).

## 1.4 Neonatal parenteral nutrition volume

- 1.4.1 [Standardised neonatal parenteral nutrition \('standardised bags'\)](#) should be formulated in concentrated solutions to help ensure that the nutritive element of intravenous fluids is included within the total fluid allowance.

For a short explanation of why the committee made this recommendation and how it might affect practice, see the [rationale and impact section on neonatal parenteral nutrition volume](#).

Full details of the evidence and the committee's discussion are in [evidence review J: general principles](#).

## 1.5 Constituents of neonatal parenteral nutrition

### Glucose

- 1.5.1 For preterm and term babies, give glucose as follows:
- If starting parenteral nutrition in the first 4 days after birth:
    - give a starting range of 6 to 9 g/kg/day
    - gradually increase (for example, over 4 days) to a maintenance range of 9 to 16 g/kg/day.
  - If starting parenteral nutrition more than 4 days after birth:

- give a range of 9 to 16 g/kg/day.

For a short explanation of why the committee made this recommendation and how it might affect practice, see the [rationale and impact section on constituents of neonatal parenteral nutrition – glucose](#).

Full details of the evidence and the committee's discussion are in [evidence review D1: glucose](#).

## Amino acids

1.5.2 For preterm babies, give amino acids as follows:

- If starting parenteral nutrition in the first 4 days after birth:
  - give a starting range of 1.5 to 2 g/kg/day
  - gradually increase (for example, over 4 days) to a maintenance range of 3 to 4 g/kg/day.
- If starting parenteral nutrition more than 4 days after birth:
  - give a range of 3 to 4 g/kg/day.

1.5.3 For term babies, give amino acids as follows:

- If starting parenteral nutrition in the first 4 days after birth:
  - give a starting range of 1 to 2 g/kg/day
  - gradually increase (for example, over 4 days) to a maintenance range of 2.5 to 3 g/kg/day.
- If starting parenteral nutrition more than 4 days after birth:
  - give a range of 2.5 to 3 g/kg/day.

For a short explanation of why the committee made these recommendations and how they might affect practice, see the [rationale and impact section on constituents of neonatal parenteral nutrition – amino acids](#).

Full details of the evidence and the committee's discussion are in [evidence review D2: amino acids](#).

## Lipids and lipid emulsions

1.5.4 For preterm and term babies, give lipids as follows:

- If starting parenteral nutrition in the first 4 days after birth:
  - give a starting range of 1 to 2 g/kg/day
  - gradually increase (for example, in daily increments of 0.5 to 1 g/kg/day) to a maintenance range of 3 to 4 g/kg/day.
- If starting parenteral nutrition more than 4 days after birth:
  - give a range of 3 to 4 g/kg/day.

1.5.5 For preterm and term babies with parenteral nutrition-associated liver disease, consider giving a [composite lipid emulsion](#) rather than a pure soy lipid emulsion.

For a short explanation of why the committee made these recommendations and how they might affect practice, see the [rationale and impact section on constituents of neonatal parenteral nutrition – lipids and lipid emulsions](#).

Full details of the evidence and the committee's discussion are in [evidence review D3: lipids](#) and [evidence review D4: lipid emulsions](#).

## Ratios of non-nitrogen energy to nitrogen, and carbohydrates to lipids

1.5.6 When giving neonatal parenteral nutrition to preterm or term babies:

- use the values for each individual component in recommendations 1.5.1 to 1.5.4
- provide non-nitrogen energy as 60% to 75% carbohydrate and 25% to 40% lipid
- use a non-nitrogen energy to nitrogen ratio in a range of 20 to 30 kcal of non-nitrogen energy per gram of amino acids (this equates to 23 to 34 kcal of total energy per gram of amino acid).

1.5.7 When altering the amount of neonatal parenteral nutrition, maintain the non-nitrogen energy to nitrogen ratio, and the carbohydrate to lipid ratio, to keep within the ranges of ratios specified in recommendation 1.5.6.

For a short explanation of why the committee made these recommendations and how they might affect practice, see the [rationale and impact section on constituents of neonatal parenteral nutrition – ratios of non-nitrogen energy to nitrogen, and carbohydrates to lipids](#).

Full details of the evidence and the committee's discussion are in

[evidence review D7: ratio of non-nitrogen energy to nitrogen](#), [evidence review D8: ratio of carbohydrates to lipids](#) and [evidence review D10: ratio of phosphate to amino acids](#).

## Iron

- 1.5.8 Do not give intravenous parenteral iron supplements to preterm or term babies on neonatal parenteral nutrition who are younger than 28 days.
- 1.5.9 For preterm babies on neonatal parenteral nutrition who are 28 days or older, monitor for iron deficiency and treat if necessary (see recommendation 1.7.11).

For a short explanation of why the committee made these recommendations and how they might affect practice, see the [rationale and impact section on constituents of neonatal parenteral nutrition – iron](#).

Full details of the evidence and the committee's discussion are in [evidence review D5: iron](#).

## Acetate

For a short explanation of why the committee did not make a recommendation, see the [rationale section on constituents of neonatal parenteral nutrition – acetate](#).

Full details of the evidence and the committee's discussion are in [evidence review D6: acetate](#).

## Calcium

1.5.10 For preterm and term babies, give calcium as follows:

- If starting parenteral nutrition in the first 48 hours after birth:
  - give a starting range of 0.8 to 1 mmol/kg/day
  - increase to a maintenance range of 1.5 to 2 mmol/kg/day after 48 hours.
- If starting parenteral nutrition more than 48 hours after birth, give a range of 1.5 to 2 mmol/kg/day.

## Phosphate

1.5.11 For preterm and term babies, give phosphate as follows:

- If starting parenteral nutrition in the first 48 hours after birth:
  - give 1 mmol/kg/day

- increase to a maintenance dosage of 2 mmol/kg/day after 48 hours.
  - If starting parenteral nutrition more than 48 hours after birth, give 2 mmol/kg/day.
  - Give a higher dosage of phosphate if indicated by serum phosphate monitoring.
- 1.5.12 Be aware that preterm babies may be at increased risk of phosphate deficit requiring additional phosphate supplementation.

## Ratio of calcium to phosphate

- 1.5.13 Use a calcium to phosphate ratio of between 0.75:1 and 1:1 for preterm and term babies on neonatal parenteral nutrition.

For a short explanation of why the committee made these recommendations and how they might affect practice, see the [rationale and impact section on constituents of neonatal parenteral nutrition – calcium and phosphate](#).

Full details of the evidence and the committee's discussion are in [evidence review D9: ratio of calcium to phosphate](#).

## Other constituents of neonatal parenteral nutrition – general principles

### Vitamins

- 1.5.14 Give daily intravenous fat-soluble and water-soluble vitamins ideally from the outset, but as soon as possible after starting parenteral nutrition, to maintain standard daily requirements.
- 1.5.15 Give fat-soluble and water-soluble vitamins in the intravenous lipid emulsion to improve their stability.

## Electrolytes

- 1.5.16 Give sodium and potassium in parenteral nutrition to maintain standard daily requirements, adjusted as necessary for the individual baby.
- 1.5.17 Be aware that even if the parenteral nutrition solution contains sodium and potassium, additional supplements of these electrolytes can be given using a separate intravenous infusion.

## Magnesium

- 1.5.18 Give magnesium in parenteral nutrition ideally from the outset, but as soon as possible after starting parenteral nutrition.

## Trace elements

- 1.5.19 Give daily intravenous trace elements ideally from the outset, but as soon as possible after starting parenteral nutrition.

For a short explanation of why the committee made these recommendations and how they might affect practice, see the [rationale and impact section on other constituents of neonatal parenteral nutrition – general principles](#).

Full details of the evidence and the committee's discussion are in [evidence review J: general principles](#).

## 1.6 Standardised neonatal parenteral nutrition formulations ('standardised bags')

- 1.6.1 When starting neonatal parenteral nutrition for preterm and term babies, use a standardised neonatal parenteral nutrition formulation ('standardised bag').

Note that this might be an off-label use as not all parenteral nutrition formulations



have a UK marketing authorisation for this indication. See [prescribing medicines](#) for more information.

1.6.2 Standardised bags should:

- be formulated to allow delivery of parenteral nutrition as recommended in the [section on neonatal parenteral nutrition volume](#) and the [section on constituents of neonatal parenteral nutrition](#)
- be prepared following nationally agreed quality standards.

1.6.3 Continue with a standardised bag unless an [individualised parenteral nutrition formulation](#) is indicated, for example, if the baby has:

- complex disorders associated with a fluid and electrolyte imbalance
- renal failure.

For a short explanation of why the committee made these recommendations and how they might affect practice, see the [rationale and impact section on standardised neonatal parenteral nutrition formulation](#).

Full details of the evidence and the committee's discussion are in [evidence review E: standardised neonatal parenteral nutrition formulations](#).

## 1.7 Monitoring neonatal parenteral nutrition

1.7.1 When taking blood samples to monitor the preterm or term baby's neonatal parenteral nutrition:

- collect the minimum blood volume needed for the tests
- use a protocol agreed with the local clinical laboratory to retrieve as much information as possible from the sample
- coordinate the timing of blood tests to minimise the number of blood samples needed.

## Blood glucose

1.7.2 Measure the blood glucose level:

- 1 to 2 hours after first starting parenteral nutrition
- 1 to 2 hours after each change of parenteral nutrition bag (usually every 24 or 48 hours).

1.7.3 Measure blood glucose more frequently if:

- the preterm or term baby has previously had hypoglycaemia or hyperglycaemia
- the dosage of intravenous glucose has been changed
- there are clinical reasons for concern, for example, sepsis or seizures.

## Blood pH, potassium, chloride and calcium

1.7.4 Measure the blood pH, potassium, chloride and calcium levels:

- daily when starting and increasing parenteral nutrition
- twice weekly after reaching a maintenance parenteral nutrition.

1.7.5 Measure blood pH, potassium, chloride or calcium more frequently if:

- the preterm or term baby has previously had levels of these components outside the normal range
- the dosages of intravenous potassium, chloride or calcium have been changed
- there are clinical reasons for concern, for example, in critically ill babies.

## Serum triglycerides

1.7.6 Measure serum triglycerides:

- daily while increasing the parenteral nutrition lipid dosage
- weekly after reaching a maintenance intravenous lipid dosage.

1.7.7 Measure serum triglycerides more frequently, but not more than once a day, if:

- the level is elevated
- the preterm or term baby is at risk of hypertriglyceridaemia, for example, if the baby is critically ill or has a lipaemic blood sample.

1.7.8 Be aware that ongoing serum triglyceride monitoring may not be needed for stable preterm or term babies transitioning from parenteral nutrition to enteral nutrition.

## Serum or plasma phosphate

1.7.9 Measure the serum or plasma phosphate level:

- daily while increasing the parenteral nutrition phosphate dosage
- weekly after reaching a maintenance intravenous phosphate dosage.

1.7.10 Consider measuring serum or plasma phosphate more frequently:

- if the level has been outside the normal range
- if there are clinical reasons for concern, for example, metabolic bone disease
- for preterm babies born at less than 32+0 weeks.

## Iron status

1.7.11 Measure ferritin, iron and transferrin saturation if a preterm baby is on parenteral

nutrition for more than 28 days.

## Liver function

1.7.12 Measure liver function weekly in preterm and term babies on parenteral nutrition.

1.7.13 Measure liver function more frequently than weekly if there are clinical concerns or previous liver function test levels outside the normal range.

For a short explanation of why the committee made these recommendations and how they might affect practice, see the [rationale and impact section on monitoring neonatal parenteral nutrition](#).

Full details of the evidence and the committee's discussion are in [evidence review F: monitoring neonatal parenteral nutrition](#).

## 1.8 Stopping neonatal parenteral nutrition

1.8.1 For all babies, take into account the following when deciding when to stop parenteral nutrition:

- the baby's tolerance of enteral feeds
- the amount of nutrition being delivered by enteral feeds (volume and composition)
- the relative contribution of parenteral nutrition and enteral nutrition to the baby's total nutritional requirement
- the likely benefit of the nutritional intake compared with the risk of venous catheter sepsis
- the individual baby's particular circumstances, for example, a baby with complex needs such as short bowel syndrome, increased stoma losses or slow growth, may need long-term parenteral nutrition.

- 1.8.2 For preterm babies born before 28+0 weeks, consider stopping parenteral nutrition within 24 hours once the enteral feed volume is 140 to 150 ml/kg/day, taking into account the factors in recommendation 1.8.1.
- 1.8.3 For preterm babies born at or after 28+0 weeks and term babies, consider stopping parenteral nutrition within 24 hours if the enteral feed volume tolerated is 120 to 140 ml/kg/day, taking into account the factors in recommendation 1.8.1.

For a short explanation of why the committee made these recommendations and how they might affect practice, see the [rationale and impact section on stopping neonatal parenteral nutrition](#).

Full details of the evidence and the committee's discussion are in [evidence review G: stopping parenteral nutrition](#).

## 1.9 Service design

- 1.9.1 Neonatal parenteral nutrition services should be supported by a specialist multidisciplinary team. Such teams could be based locally or within a clinical network.
- 1.9.2 The neonatal parenteral nutrition multidisciplinary team should include a consultant neonatologist or paediatrician with a special interest in neonatology, a neonatal pharmacist and a neonatal dietitian, and should have access to the following:
- a neonatal nurse
  - a paediatric gastroenterologist
  - an expert in clinical biochemistry.
- 1.9.3 The neonatal parenteral nutrition multidisciplinary team should be responsible for:
- governance, including:
    - agreeing policies and protocols for the neonatal parenteral nutrition

service

- ensuring that policies and protocols for neonatal parenteral nutrition are followed and audited
- monitoring clinical outcomes
- supporting delivery of parenteral nutrition, including:
  - providing clinical advice
  - providing enhanced multidisciplinary team input for preterm and term babies with complex needs, for example, babies with short bowel syndrome who may need long-term parenteral nutrition.

For a short explanation of why the committee made these recommendations and how they might affect practice, see the [rationale and impact section on service design](#).

Full details of the evidence and the committee's discussion are in [evidence review H: service design](#).

## 1.10 Information and support for parents and carers

- 1.10.1 Ask parents and carers of babies on parenteral nutrition how and when they would like to receive information and updates, and how much information they would like about their baby's care.
- 1.10.2 Topics to discuss with parents or carers include:
- why their baby needs parenteral nutrition
  - what parenteral nutrition involves
  - the importance of good nutrition for newborn babies
  - how long their baby is likely to need parenteral nutrition for
  - common concerns, for example, central venous catheter placement, the risk

of catheter-related infections, taking blood samples, and whether they can hold and care for their baby

- simultaneous enteral feeding, unless this is not possible
- how their baby's progress will be monitored
- how their baby will be weaned off parenteral nutrition.

1.10.3 Give information to parents or carers that:

- is tailored to their baby's circumstances
- meets their needs and preferences
- is up to date, relevant and consistent between healthcare professionals
- is available in suitable formats (written and spoken, with information available to take away).

For more guidance on communication (including different formats and languages), providing information, and shared decision making, see the [NICE guidelines on patient experience in adult NHS services, babies, children and young people's experience of healthcare and shared decision making](#).

1.10.4 Provide regular opportunities and time for parents and carers of babies on parenteral nutrition to discuss their baby's care, ask questions about the information they have been given, and discuss concerns.

For a short explanation of why the committee made these recommendations and how they might affect practice, see the [rationale and impact section on information and support for parents and carers of babies who need neonatal parenteral nutrition](#).

Full details of the evidence and the committee's discussion are in [evidence review I: information and support](#).

## Terms used in this guideline

This section defines terms that have been used in a particular way for this guideline.

### Composite lipid emulsion

A lipid emulsion that is derived from more than 1 source, for example, it might include 2 or more of soy oil, medium chain triglycerides, olive oil or fish oil.

### Individualised parenteral nutrition formulations

Aqueous and lipid parenteral nutrition solutions that meet the nutritional requirements of an individual baby. The solutions are not pre-formulated and have to be prescribed and made up each time they are needed, on an individual basis for each baby. Electrolytes can be added, and macronutrients or micronutrients can be adjusted as necessary.

### Nominal group consensus method

This is a structured method focusing on the opinions of individuals within a group to reach a consensus. Because of the focus on individuals, it is referred to as a 'nominal group' technique. It involves anonymous voting with an opportunity to provide comments. Options with low agreement are eliminated and options with high agreement are retained. Using the comments that individuals provide, options with medium agreement are revised and then considered in a second round.

### Osmolality or osmolarity

Measurement of the number of dissolved particles present in a solution to indicate fluid concentration. It is defined as the number of osmoles of solute per kilogram of solvent (osmolality), or the number of osmoles of solute per litre of solution (osmolarity).

### Preterm

A baby born before 37+0 weeks. This can be subdivided further:

- extremely preterm: babies born at less than 28+0 weeks
- very preterm: babies born at between 28+0 and 31+6 weeks



- moderate to late preterm: babies born at between 32+0 and 36+6 weeks.

## **Standardised neonatal parenteral nutrition formulations ('standardised bags')**

Standardised bags contain pre-formulated aqueous and lipid parenteral nutrition solutions made to a set composition that is not varied. They are ready to use and aim to meet the nutritional and clinical needs of a defined group of babies. Additional intravenous infusions are sometimes used to meet more individualised fluid or electrolyte requirements.

Standardised bags are prescribed as part of a standardised parenteral nutrition regimen: a choice of standardised bags that are given at the appropriate volume to meet the nutritional and clinical needs of a defined group of babies.

# Recommendations for research

The guideline committee has made the following key recommendations for research.

## 1 Information and support

What are the information and support needs of parents and carers with babies on parenteral nutrition?

For a short explanation of why the committee made the recommendation for research, see the [rationale section on information and support for parents and carers of babies who need neonatal parenteral nutrition](#).

Full details of the evidence and the committee's discussion are in [evidence review I: information and support](#).

## 2 Ratios of non-nitrogen energy to nitrogen

What is the optimal ratio of non-nitrogen energy to nitrogen in parenteral nutrition for preterm and term babies?

For a short explanation of why the committee made the recommendation for research, see the [rationale section on constituents of neonatal parenteral nutrition – ratios of non-nitrogen energy to nitrogen, and carbohydrates to lipids](#).

Full details of the evidence and the committee's discussion are in [evidence review D7: ratio of non-nitrogen energy to nitrogen](#).

## 3 Timing of starting neonatal parenteral nutrition

What is the optimal timeframe for starting parenteral nutrition in term babies who are critically ill or require surgery?

For a short explanation of why the committee made the recommendation for research, see the [rationale section on indications for, and timing of, neonatal parenteral nutrition](#).

Full details of the evidence and the committee's discussion are in [evidence review A2: optimal timeframe to start parenteral nutrition](#).

## 4 Venous access

What overall osmolality (or concentration of calcium and glucose/dextrose) in parenteral nutrition can determine whether to administer centrally or peripherally?

For a short explanation of why the committee made the recommendation for research, see the [rationale section on administration of neonatal parenteral nutrition](#).

Full details of the evidence and the committee's discussion are in [evidence review B: venous access](#).

## Rationale and impact

These sections briefly explain why the committee made the recommendations and how they might affect services. They link to details of the evidence and a full description of the committee's discussion.

## Indications for, and timing of, neonatal parenteral nutrition

Recommendations 1.1.1 to 1.1.6

### Why the committee made the recommendations

#### Indications for starting neonatal parenteral nutrition (recommendations 1.1.1 to 1.1.3)

There was no evidence on the indications for neonatal parenteral nutrition, and limited evidence about the timeframe in which it should be provided, so the committee used their knowledge and experience to make the recommendations.

The committee agreed that all preterm babies born before 31+0 weeks should receive parenteral nutrition from birth until they transition to enteral feeds. Even though there was no specific evidence for this, the committee agreed that there is a risk of significant deficits in nutrition and short-term and long-term adverse events if babies born before 31+0 weeks are not supported by parenteral nutrition from birth.

For preterm babies born at or after 31+0 weeks, it needs to be established whether sufficient progress is made with enteral feeding within the first 72 hours after the birth. The committee decided not to be prescriptive about 'sufficient', to reflect the clinical judgements that healthcare professionals would make depending on each baby's individual circumstances and condition, and because enteral nutrition was not reviewed as part of this guideline. If babies have difficulties tolerating enteral feeds during this time, parenteral nutrition should be provided without delay. The committee was aware of evidence that this group of moderately preterm babies is at increased risk of long-term neurodevelopmental problems, and that optimal early nutrition may reduce the risk.

The committee discussed the influence of gestational age and birthweight on gut maturity and the baby's ability to tolerate enteral feeds. Although weight is closely linked to age, the committee had concerns that including more than 1 parameter may lead to uncertainty in deciding when to start parenteral nutrition, so they based the recommendations solely on gestational age at birth.

Critically ill term babies (with, for example, sepsis), and babies with congenital disorders, may be unlikely to make progress on enteral feeding. The committee agreed that this would be a clinical judgement, depending on each baby's circumstances and condition. They agreed that a delay could have long-term consequences and recommended parenteral feeding for these babies.

### **Indications for starting neonatal parenteral nutrition if enteral feeds are stopped (recommendations 1.1.4 and 1.1.5)**

The committee agreed the timings based on their knowledge and experience, and because preterm babies have limited stores and the potential for accumulating deficits. For term babies, the committee based the recommendation on current practice and their knowledge of the more replete nutritional stores of a baby born at term.

### **Timing of starting parenteral nutrition (recommendation 1.1.6)**

There was evidence to show that, for preterm babies, there are some benefits to starting parenteral nutrition early. However, the definition of 'early' varied in the evidence (ranging from 2 hours to 36 hours without very clear descriptions of the enteral feeding regimen), and there was no consistent pattern of findings. There was evidence for critically ill term babies that compared starting parenteral nutrition early (within 24 hours) with starting it after 1 week. There were some benefits in delaying parenteral nutrition but the committee had reservations about the evidence because the study was relatively small, the parenteral nutrition regimens used were not consistent across the different study sites and the intervention may not have been appropriate because parenteral nutrition would not normally be started on day 1 for critically ill term babies due to restricted fluid volumes and strain on organ systems. The timeframe for starting parenteral nutrition is therefore based on what the committee believe is achievable and safe.

The committee agreed that starting parenteral nutrition within 8 hours of the decision being made to provide it would reduce the risks of a nutritional deficit developing for the smallest babies (born at less than 31+0 weeks). In addition, the committee noted that this

timeframe would allow for placement of central lines if needed.

The committee also discussed the timeframe for critically ill babies, but there was not enough evidence to make a separate recommendation. From their knowledge and experience, they were aware that without parenteral nutrition, preterm babies will develop a nutritional deficit more rapidly than term babies who have greater nutritional reserves; therefore, they agreed that it may take longer to decide whether parenteral nutrition in term babies is needed.

However, once the decision is made that parenteral nutrition is needed, it should be started within 8 hours, regardless of whether babies are term or preterm.

The committee recognised the need for further research to inform the timing of starting parenteral nutrition for term babies who are critically ill or require surgery.

## **How the recommendations might affect practice**

The committee agreed that the recommendations would improve consistency of care across neonatal units, and ensure that the nutritional needs of vulnerable babies are met. Hospitals providing care for babies for whom parenteral nutrition is indicated would have to provide access to parenteral nutrition. If a hospital does not have access to neonatal parenteral nutrition, babies would need to be transferred to a unit that could provide it.

Early provision may be more costly because parenteral nutrition and staff would need to be available out-of-hours (including during weekends) to administer parenteral nutrition within the first 8 hours. However, costs can be reduced by using standardised parenteral nutrition bags, as recommended in the [section on standardised neonatal parenteral nutrition formulations \('standardised bags'\)](#), which can be stored and be readily accessible. The committee believe that there should be no reason why neonatal units cannot stock standardised bags because they have a long enough shelf life to enable storage, as long as a system of stock rotation is in place. The committee also agreed that the costs of early administration would be offset by the positive impact of early optimal nutrition.

Full details of the evidence and the committee's discussion are in:

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# Administration of neonatal parenteral nutrition

## Recommendations 1.2.1 to 1.2.3

### Why the committee made the recommendations

#### **Venous access (recommendations 1.2.1 and 1.2.2)**

There was some evidence that included a comparison of fluid concentrations (as measured by osmolality or osmolarity, which depends on the level of calcium and glucose within the same amount of fluid) for peripheral venous lines. This evidence included delivering peripheral parenteral nutrition at concentrations of up to 1,425 mOsm/l. However, the committee agreed that it was not possible to recommend a specific safe concentration for parenteral nutrition delivered peripherally because of the wide range of concentrations used in the different groups in the study. Furthermore, there was no evidence that compared centrally with peripherally inserted catheters for any given level of concentration of parenteral nutrition. Therefore, the committee made their recommendations using the available evidence, as well as their knowledge and experience.

The committee discussed the risks and benefits associated with centrally and peripherally inserted catheters. The committee acknowledged that there is variation in clinical practice, and some units routinely use peripherally inserted catheters, whereas others prefer centrally inserted catheters and avoid using peripherally inserted catheters.

The committee agreed that centrally inserted catheters should normally be the preferred option for delivering neonatal parenteral nutrition. This is because centrally inserted catheters have a longer lifespan, and the central vein is bigger and has a lower risk of thrombophlebitis. However, they also agreed that peripherally inserted catheters can be used safely (which was supported by the evidence) when use of a peripheral line will be short term, and should be used when parenteral nutrition would otherwise be delayed or interrupted (for example, because there is no one available to insert a central venous catheter, a central venous catheter has stopped working and needs to be removed, or there are concerns about line infection). The committee did not define how long parenteral nutrition can be delayed before peripheral venous access should be considered, because this decision will be based on clinical judgement. Ideally, delays should not exceed the 8 hours specified in recommendation 1.1.6, but healthcare professionals will need to consider the risks and benefits of inserting a peripheral line if it is anticipated that a

central venous catheter would be inserted soon.

The benefits and risks of surgically inserted central catheters were also discussed by the committee, and recommendations were made that these should only be used in exceptional circumstances when non-surgical insertion is not possible, or it is expected that parenteral nutrition would be needed for a long time.

Because of the limited evidence, the committee decided to prioritise this topic for further research. This is important because peripheral lines (although not the preferred choice of the committee) are generally easier to insert, and are very commonly used for a number of indications on neonatal units. However, they have a shorter life span and therefore would need to be changed more frequently. Because the infusions run into a smaller peripheral vein, there is a greater risk of the infusion causing direct damage to the vein. This is particularly true if there is a higher concentration (as measured by osmolality or osmolarity, depending on the unit of measurement) of the parenteral nutrition infusion fluid, for example, a formulation with a higher dextrose load.

### **Protection from light (recommendation 1.2.3)**

Photo-degradation and oxidation are processes that do not lend themselves to comparative clinical studies (because of safety risks if the integrity of the solution is compromised) that are commonly used as evidence in NICE guidelines, so the committee made the recommendation based on a formal nominal group consensus method and their knowledge and experience.

The committee discussed photo-degradation and oxidation of parenteral nutrition solutions (including aqueous and lipid components), which can be managed by protecting both the infusion set (tubing) and bag from light. The committee discussed whether to recommend protecting just the bag, or the bag, the tubing and syringe. They recognised that it is simple to cover the bag, and this is already done in current practice. The committee agreed that, although some units would need to use a different type of infusion set, it is best practice to also protect the infusion set and syringe of both aqueous and lipid parenteral nutrition solutions from light, in line with European Medicines Agency and Medicines and Healthcare products Regulatory Agency guidance that states 'for administration to neonates and children below 2 years of age, parenteral nutrition products containing amino acids and/or lipids should be protected from light (containers and administration sets)'.<sup>1</sup>



## **Filtration**

The committee acknowledged that adding a terminal filter to the infusion set makes giving parenteral nutrition significantly more expensive. They discussed that adding filters can remove particulate matter, fungi, bacteria and endotoxins depending on the size of the filter. However, making up parenteral nutrition in aseptic units and using bags instead of syringes reduces the risk of bacterial contamination. Breaking a line to change the filter when running lipid from a bag was thought to pose more of an infection risk than changing the bag and filter frequently (every 48 hours). Given these uncertainties around benefits and harms, as well as additional costs, the committee were not able to make a recommendation related to filtration.

## **How the recommendations might affect practice**

### **Venous access**

The recommendations reinforce current best practice. The recommendations may affect clinical practice by reducing the current delay that some units experience when siting a central line for giving parenteral nutrition, because peripherally inserted catheters may now be used as a short-term alternative.

### **Protection from light**

Any likely changes in practice and costs associated with light-protected bags and light-protected tubing will be outweighed by the benefits associated with preserving the integrity of the parenteral nutrition solution.

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## **Energy needs of babies on neonatal parenteral nutrition**

[Recommendations 1.3.1 to 1.3.3](#)

### **Why the committee made the recommendations**

There was limited evidence on the energy needs for babies on parenteral nutrition, so the

committee used their knowledge and experience to give a starting and maintenance range, and an example of how this should be increased gradually. The committee discussed the number of days over which energy intake should increase to reach the intended maintenance level, and agreed to align this with the recommendations on lipid, glucose and amino acid increases.

The committee agreed that babies who start parenteral nutrition in the first 4 days after birth should have a starting range and increase up to a maintenance range over approximately 4 days. This timeframe was primarily selected because neonatal metabolic adaptation occurs in the early days of life, enabling the baby to metabolise the nutrients delivered. In addition, fluid volume allowances are commonly increased over the first few days of life and this allows increasing amounts of nutrition to be given parenterally.

For babies who start parenteral nutrition more than 4 days after birth, early metabolic adaptation is likely to have taken place. The fluid allowances will have already increased, so this allows parenteral nutrition to be started using maintenance ranges.

The energy requirements were taken from the committee's knowledge, informed (to a limited extent) by the evidence, and cross-referenced to the energy delivered by the combined constituent components (in the [section on constituents of neonatal parenteral nutrition](#)).

The committee agreed that giving energy at the lower range may be more appropriate for term babies who are critically ill or have just had surgery because the energy stores of term babies tend to be more replete. However, in critically ill preterm babies, who have limited nutritional stores, prioritising nutritional intake may be more important.

## **How the recommendations might affect practice**

The committee agreed that the recommendations would improve consistency of care across neonatal units and would not incur extra costs or increase resource use. Providing the appropriate nutritional intake may avoid additional costs associated with nutritional deficit or providing excess energy.

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# Neonatal parenteral nutrition volume

## Recommendation 1.4.1

### **Why the committee made the recommendation**

The recommendation on parenteral nutrition fluid volume was not developed by the usual NICE guideline systematic review process. The committee agreed the recommendation using a formal nominal group consensus method as well as their knowledge and experience.

The total fluid requirement for preterm and term babies is a complex topic, and was outside the scope of this guideline. Nevertheless, it is an important factor in providing neonatal parenteral nutrition. In some situations, the total fluid allowance may be restricted, or a significant proportion of the allowance might be required for other purposes (for example, other intravenous drug infusions). The committee recognised that this could result in difficulties in giving the required amount of parenteral nutrition. In order to minimise this risk, the committee agreed that standardised neonatal parenteral nutrition formulations ('standardised bags') should use the smallest fluid volume possible (see the [section on standardised neonatal nutrition formulations](#)). Concentrating parenteral nutrition in this way will facilitate the provision of nutritional requirements within the total fluid allowance.

### **How the recommendation might affect practice**

The committee agreed that the recommendation will reinforce current best practice.

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# Constituents of neonatal parenteral nutrition – glucose

## Recommendation 1.5.1

### **Why the committee made the recommendation**

The evidence on glucose was difficult to interpret and draw any conclusions from. Only

1 study has been conducted that varied glucose intake without also varying other constituents (such as amino acids and lipids), so it is difficult to see what effect different levels of glucose intake have. Because of this, the committee used their knowledge and experience of physiological and metabolic requirements, and took into account the glucose doses used in the studies as well as current practice and international guidelines, when making their recommendation.

The committee decided that the maintenance range should be given for babies who start parenteral nutrition more than 4 days after birth. This is consistent with the approximate 4 days by which a maintenance dosage would be reached in babies starting parenteral nutrition from birth, because tolerance would increase during the first few days of life.

## **How the recommendation might affect practice**

The committee agreed that the recommendation will reinforce current best practice.

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# **Constituents of neonatal parenteral nutrition – amino acids**

[Recommendations 1.5.2 and 1.5.3](#)

## **Why the committee made the recommendations**

There was a lot of evidence related to amino acid intake. However, the evidence was uncertain, for example, because the studies involved small numbers of babies and the results were inconsistent, so the committee also used their knowledge and experience of current practice to make the recommendations.

For preterm babies, 1.5 g/kg/day was chosen as the lower starting dose threshold, because less than this can result in a negative nitrogen balance. The committee did not look for evidence on how different amino acid doses affect nitrogen balance, but used their knowledge of metabolic studies, which are widely used to estimate the minimum amount of amino acids needed to prevent negative nitrogen balance. The upper starting dose threshold of 2 g/kg/day was selected because there was evidence of better growth at a starting dose of 2 g/kg/day of amino acids compared with less than 2 g/kg/day, but

these benefits did not persist at higher amino acid starting doses (3 g/kg/day).

Studies using different maximal amino acid intakes were considered in the evidence review, and informed the recommended maintenance range. There was some evidence that a maximal amino acid intake of 3 g/kg/day or more compared with less than 3 g/kg/day improved growth outcomes, but there was no evidence of reduced sepsis or neurodevelopmental problems. There was some evidence of appropriate growth at a maximal intake of 2.7 g/kg/day, but this was supported by early (within the first 24 hours) and progressive enteral feeding. Some babies receiving neonatal parenteral nutrition will be on no or minimal enteral feeds, or will be unable to increase enteral feeding in a timely manner. This, combined with the weak evidence of improved growth at 3 g/kg/day or more, meant that 3 g/kg/day was selected as the lower end of the maintenance range. However, the committee were split on this point so a majority decision was taken.

The committee agreed, based on their expertise, that it was important to provide an upper limit for amino acid intake because of possible adverse events such as acidosis, high serum urea, hypercalcaemia or hypophosphatemia, hypokalaemia and re-feeding syndrome. The maximal amino acid intake in the studies reviewed was 4 g/kg/day. The committee looked for adverse effects across all the studies in the evidence review, including those using maximal amounts of over 3.5 g/kg/day, and found no evidence of harm. However, the committee were concerned that the absence of evidence of harm is not the same as evidence of absence. It was noted that higher amino acid intakes need to be supported by sufficient non-nitrogen energy. The committee followed the evidence in agreeing an upper maintenance range limit of 4 g/kg/day. They suggested being more vigilant for adverse effects when using the top half of this maintenance range.

Babies on enteral feeds will receive macronutrients from milk in addition to those from parenteral nutrition. The committee acknowledged that for those babies on enteral feeds, the proportional decrease in parenteral nutrition as enteral intake increases will decrease the delivery of amino acids from parenteral nutrition, thus alleviating risks of excessive amino acid delivery. However, they noted that the enteral feeding regimen was outside the scope of this guideline, so did not recommend different ratios for babies on enteral feeds.

Most of the studies gradually increased amino acid intake over a number of days to reach a target dose. However, there was not enough consistent evidence to specify the number of days over which intake should be increased. The committee recommended 4 days, based on informal consensus agreement, using their knowledge and experience. In addition, the committee agreed that this is approximately how long it would take to reach

the maintenance range if incrementing from the starting range at rates similar to those used in the included studies. This also matched the recommendations made for glucose and lipids, which is important because nitrogen to non-nitrogen ratios need to be maintained within the range specified in the guideline.

There was no evidence about amino acids for term babies, so the committee recommended a lower starting and maintenance dose based on their own expert consensus and knowledge of nitrogen balance studies. These studies show that term babies lose less protein than preterm babies, and suggest the amount of amino acids needed to achieve similar weight gain to term babies on milk feeds.

There was no evidence for babies who did not start parenteral nutrition from birth. The committee agreed, based on their expertise, that babies starting parental nutrition more than 4 days after birth would be able to tolerate the maintenance dosage of amino acids.

## **How the recommendations might affect practice**

The committee noted that the recommendations will reduce variation in practice.

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# **Constituents of neonatal parenteral nutrition – lipids and lipid emulsions**

[Recommendations 1.5.4 and 1.5.5](#)

## **Why the committee made the recommendations**

The evidence was uncertain (there was an inconsistent pattern of benefit and harm), so the committee also used their knowledge and experience of current practice to make the recommendations by informal consensus.

There was evidence of both benefit and harm when giving lipids compared with no lipids, but the committee agreed that the benefits of giving lipids outweighed possible risks. There was evidence that giving lipids in the ranges provided in the studies was not associated with any harm in the short term. In addition, there was evidence that higher doses may reduce retinopathy of prematurity and necrotising enterocolitis compared with

lower doses. The committee concluded that the ranges in the studies were safe and effective.

In relation to how the target dose is reached, the evidence showed that 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, compared with starting at a higher dose and rapidly increasing to the same target dose. The committee agreed to use similar parameters in the recommendations. Based on their knowledge of doses of lipids exceeding those used in the studies and the risk of problems such as hypertriglyceridemia, the committee recommended an upper limit for the maintenance dose.

The committee recommended that in babies with parenteral nutrition-associated liver disease, consideration be given to changing from a pure soy lipid emulsion (if that is being used) to a composite lipid emulsion. The committee discussed some evidence suggesting that there was more resolution of parenteral nutrition-associated liver disease or cholestasis with fish oil-containing lipid emulsions compared with pure soy lipid emulsions. However, the committee noted that there were limitations in the design of some studies and uncertainty in the measurement, which made this evidence very weak. There was also some evidence of a benefit with pure fish oil, but the committee were aware that there is a risk of essential fatty acid deficiency with pure fish oil. They therefore decided that even though this evidence to support the efficacy of composite lipid emulsions is not compelling, it could be trialled because these babies are at risk of developing progressive liver disease and liver failure. The available evidence was from preterm and late preterm babies. However, the recommendation was extended to cover term babies based on expertise from the committee that late preterm and term babies often have the same treatment, and similar benefits would be likely for term babies.

The committee did not make recommendations for babies with surgical conditions because there was no evidence of advantage of any type of lipid emulsion over other lipid formulations. Recommendations were not made for babies without parenteral nutrition-associated liver disease, including those at high risk, because there was not conclusive evidence of either benefit or harm.

## **How the recommendations might affect practice**

The committee agreed that the recommendations will reinforce and standardise current best practice.

Full details of the evidence and the committee's discussion are in:

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## **Constituents of neonatal parenteral nutrition – ratios of non-nitrogen energy to nitrogen, and carbohydrates to lipids**

[Recommendations 1.5.6 and 1.5.7](#)

### **Why the committee made the recommendations**

#### **Ratio of non-nitrogen energy to nitrogen**

There was limited evidence, and the evidence did not provide sufficient data to inform optimal ratios. The committee used their knowledge and experience to agree ratios, taking into account the available evidence and current practice.

When the amount of parenteral nutrition is changing (for example, when transitioning onto enteral feeding), there is a risk of negative outcomes associated with too low or too high ratios. Too low a ratio (non-nitrogen energy to nitrogen below 20 kcal per gram) could cause oxidation of amino acids and high blood urea. Too high a ratio (non-nitrogen energy to nitrogen above 30 kcal per gram) could result in deposition of excess body fat, which is associated with metabolic ill health in later life (for example, risk of cardiovascular disease, diabetes and obesity-related conditions). Because of these risks, the committee recommended keeping the ratios the same when changing the amount of parenteral nutrition.

The evidence supported the need to give babies enough energy to ensure the nitrogen provided is retained.

Because of the limited evidence, the committee decided to prioritise this topic for further research. This is important because insufficient non-nitrogen energy (carbohydrates and lipids) leads to nitrogen (protein) being used for non-growth purposes so is not available to generate new tissues. An excess of non-nitrogen energy can lead to increased adiposity and may cause hyperglycaemia or hypertriglyceridemia. Having more evidence about the



optimal ratio of non-nitrogen energy to nitrogen in parenteral nutrition is therefore needed.

### **Ratio of carbohydrates to lipids**

There was limited evidence, so the committee used their knowledge and experience to agree the ratio, taking into account the available evidence and current practice. One study provided lipids in a range from 18% to 40% (meaning that the other 82% to 60% of non-nitrogen energy was made up of glucose), with better growth associated with 40% lipid intake.

The committee also discussed the recommendations developed for glucose and lipid dosages (recommendations 1.5.1 and 1.5.4). They agreed that it should be clear to those prescribing parenteral nutrition that when calculating the relative amounts of carbohydrate and lipid, the recommended dosages of each of these components should not be exceeded.

The committee decided not to recommend the lower end of the lipid range (18%) that was used in the evidence because that would lead to a high glucose intake, for which the risk of hyperglycaemia was considered to be too high. Therefore, the committee agreed that a lower level of 25% lipid is needed to limit the risk of hyperglycaemia, and to provide sufficient essential fatty acids and fat-soluble vitamins. The committee agreed, based on their knowledge and experience, that there should be an upper limit of 40% fat. Even though there is no evidence available to firmly state the risks of higher lipid provision, the committee agreed 40% would be safe and not risk fatty liver or raised triglyceride levels.

The recommended ranges aim to provide sufficient lipid energy to optimise growth, provide essential fatty acids and fat-soluble vitamins, and minimise the risk of hyperglycaemia. However, it is important not to give too much lipid because this could risk high triglyceride levels, fatty liver and increased fat deposition.

### **Why the committee did not make a recommendation on ratios of phosphate to amino acids**

The evidence on the relative amounts of amino acids and phosphate to be given in parenteral nutrition was limited.

The committee agreed that the phosphate to amino acid ratios derived from following the phosphate and amino acid recommendations (1.5.11, 1.5.2 and 1.5.3) in this guideline are

appropriate. However, because the evidence was limited and did not provide enough detail on the exact amount of phosphate needed per gram of amino acid, the committee decided not to make a recommendation on specific relative amounts.

## **How the recommendations might affect practice**

The committee agreed that the recommendations reflect current best practice and should have little impact on practice. They should reduce any variation across units.

Full details of the evidence and the committee's discussion are in:

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## **Constituents of neonatal parenteral nutrition – iron**

[Recommendations 1.5.8 and 1.5.9](#)

### **Why the committee made the recommendations**

There was limited evidence about intravenous iron supplementation for babies younger than 28 days. The evidence did not show a substantial benefit or harm. The committee recognised that usual clinical practice in the UK is not to include intravenous iron in the parenteral nutrition regimen for babies younger than 28 days, and agreed that there was not enough new evidence to change current practice. In addition, preterm babies often have blood transfusions that can result in unpredictable amounts of iron. The committee discussed the potential for iron overload and toxicity, and used their expertise and experience to recommend that early supplementation should not be used.

The committee agreed that healthcare professionals may need to reconsider iron supplementation for preterm babies who are 28 days or older based on monitoring for iron deficiency.

### **How the recommendations might affect practice**

The recommendations reflect current practice, so should not result in any changes.

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## Constituents of neonatal parenteral nutrition – acetate

### Why the committee decided not to make a recommendation

There was some evidence that using acetate in parenteral nutrition reduces the risk of hyperchloraemia, but there was no evidence about the amount of acetate needed. The evidence did not explain how chloride had been provided and the committee were unconvinced that the interventions used in the studies reflect current practice. The committee agreed that using the right balance of parenteral nutrition components and the use of standardised bags would avoid an excess of chloride and the need to add acetate.

The committee acknowledged that parenteral nutrition is not the only source of chloride (for example, some trace elements are in the form of chloride salts), so an imbalance may need to be addressed by adding acetate to reduce the risk of metabolic acidosis secondary to hyperchloraemia. The committee discussed that there is variation in clinical practice about the use of acetate but agreed that the evidence was not strong enough to make any recommendations about acetate.

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## Constituents of neonatal parenteral nutrition – calcium and phosphate

[Recommendations 1.5.10 to 1.5.13](#)

### Why the committee made the recommendations

#### Calcium and phosphate (ratio and absolute amounts)

Evidence was limited, and there was inconsistency in the definitions of high and low levels or concentrations of calcium and phosphate across the included studies, so the committee also used their knowledge and experience to make the recommendations.

Although the evidence that was reviewed focused on relative amounts, the committee decided that recommendations for absolute values were also needed because the amounts of calcium and phosphate in the evidence reviewed were lower than those currently given in UK clinical practice. However, the evidence also showed that higher amounts of calcium and phosphate were beneficial in reducing the incidence of rickets, fractures and hypercalciuria, and increasing bone mineral density. This guided the committee to agree that higher amounts of calcium and phosphate are preferable for preterm and term babies. They decided that a decision about the absolute amounts would then determine the ratio between these constituents rather than the other way around.

The committee made recommendations for an initial and maintenance dosage and dosage range of calcium and phosphate that overlap, which means that this would lead to a ratio between of 0.75:1 and 1:1. The committee recommended total amounts and a ratio of calcium to phosphate according to the timing of when babies would start parenteral nutrition after birth (before or after the first 48 hours) rather than whether or not they are preterm or term. This is because of body fluid adjustments in the first days of life. A too low or too high amount of calcium and phosphate and the ratio between them will result in suboptimal bone mineralisation and urinary losses. They noted that preterm babies may need more calcium and phosphate, based on their knowledge, fetal accretion studies and potential urinary phosphate losses. However, they decided not to make different recommendations for preterm or term babies because blood monitoring will indicate whether this is needed.

The committee also agreed to be more prescriptive in recommending absolute amounts of phosphate by restricting the dose to set amounts instead of a range. This was because of practical considerations: in most current parenteral preparations, 2 mmol of sodium would be administered for every 1 mmol of phosphate, and higher sodium intakes would not be recommended within the first 48 hours, before the expected postnatal diuresis. More flexibility could be applied in the amount of calcium given to babies because calcium would not alter other electrolyte delivery. The amounts of both calcium and phosphate would also be restricted by stability issues, but the committee noted that the amounts recommended could be achieved within these restrictions.

## How the recommendations might affect practice

The recommendations on phosphate and calcium are largely in line with existing guidance and reflect current best practice. There is variation in practice so the recommendations should ensure consistency of care across different care settings.

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## Other constituents of neonatal parenteral nutrition – general principles

[Recommendations 1.5.14 to 1.5.19](#)

### Why the committee made the recommendations

The recommendations were not developed by the usual NICE guideline systematic review process. The committee agreed the recommendations' evidence statements using a formal nominal group consensus method, and based the recommendations on their knowledge and experience.

#### Vitamins (recommendations 1.5.14 and 1.5.15)

The committee agreed that vitamins are an essential part of a baby's nutritional needs, and discussed whether vitamins should be provided daily. Babies gain most of their vitamin reserves from their mother in the third trimester of pregnancy, so babies born preterm are relatively vitamin deficient. The committee decided that daily vitamins would improve the vitamin accretion rate and represent best clinical practice. The committee agreed that the recommendation would apply to term babies, because term babies who need parenteral nutrition are likely to have surgical problems or to be critically unwell, so will not establish enteral feeding rapidly. In addition, there was no consensus about making a separate recommendation for term babies. Although the committee acknowledged that some initial or 'starter' parenteral nutrition preparations may not contain vitamins, they stressed that starting parenteral nutrition should not be delayed.

Putting fat- and water-soluble vitamins in the lipid emulsion improves their stability but shortens the shelf life of the lipid emulsion. However, the committee decided that ensuring vitamin stability was important and putting the vitamins in the lipid emulsion was therefore recommended. The committee noted that modern parenteral nutrition preparations generally have longer shelf lives, and so this was a smaller concern than in the past.

#### Electrolytes (recommendations 1.5.16 and 1.5.17)

Serum sodium and potassium levels can change frequently in babies on neonatal units,

and these changes may not be related to parenteral nutrition. How often sodium and potassium levels need to be checked depends on multiple factors and will be decided by the local clinical team based on the overall clinical situation. Sodium and potassium supplementation, in addition to that already contained in parenteral nutrition in phosphate (which is often given as sodium glycerophosphate), can be given using an additional intravenous infusion. This allows standardised parenteral nutrition bags to contain sufficient sodium and potassium to cover usual daily maintenance requirements but allows adjustments to sodium and potassium delivery to cover additional requirements without having to interfere with the parenteral nutrition.

### **Magnesium (recommendation 1.5.18)**

The committee agreed that magnesium is an essential component of parenteral nutrition because of its important role in skeletal development and in nervous system and muscle membranes. Although the committee noted that magnesium may not be immediately available in some initial or 'starter' parenteral nutrition preparations, they stressed that parenteral nutrition should not be delayed, and magnesium should be added as soon as possible after starting parenteral nutrition.

### **Trace elements (recommendation 1.5.19)**

The committee agreed that trace elements are an essential component of parenteral nutrition. Although the committee noted that trace elements may not be immediately available in some initial or 'starter' parenteral nutrition preparations, they stressed that parenteral nutrition should not be delayed and trace elements should be added as soon as possible after starting parenteral nutrition.

## **How the recommendations might affect practice**

The committee agreed that the recommendation will reinforce current best practice.

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## **Standardised neonatal parenteral nutrition formulation ('standardised bags')**

[Recommendations 1.6.1 to 1.6.3](#)

## Why the committee made the recommendations

There was limited evidence on whether healthcare professionals should use parenteral nutrition formulations that are standardised ('standardised bags') or individualised. The committee used the limited evidence, and their knowledge and experience, to make the recommendations.

The committee agreed that healthcare professionals should use standardised bags routinely because:

- standardised bags are immediately available when needed, and suitable for most babies
- they help to minimise prescribing errors and clinical variation
- they can improve compliance with national recommendations on quality control of parenteral nutrition manufacturing, dispensing, prescribing and administration, because they must comply with nationally agreed quality standards (in line with the [Royal Pharmaceutical Society and NHS Pharmaceutical Quality Assurance Committee standards for the quality assurance of aseptic preparation services](#))
- they have lower acquisition costs.

Individualised bags are not immediately available on a neonatal unit and are more complex to prescribe. The committee agreed that without good evidence to support the use of individualised bags, the additional complexity and cost is not justified.

Although the committee agreed that standardised bags should be used routinely and continued once started, individualised parenteral nutrition may be needed for babies with complex needs, for example, babies with a fluid imbalance.

Standardisation of parenteral nutrition is a concept which means that its effectiveness depends on optimal content for the average baby and its safety is related to the process of standardisation. Although there was some evidence suggesting that growth-related outcomes favoured an individualised approach, these findings were largely dependent on the specifics of what was in the standardised bag being trialled (which for most studies was not what would currently be recommended). The committee therefore agreed that, to be effective formulations, the standardised bags would be made up using the constituents outlined in the [section on constituents of neonatal parenteral nutrition](#) to provide optimal nutrition.

## How the recommendations might affect practice

The committee agreed that the recommendations will lead to greater consistency in clinical practice and improve safety through compliance with national recommendations for parenteral nutrition manufacturing, dispensing, prescribing and administration.

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## Monitoring neonatal parenteral nutrition

[Recommendations 1.7.1 to 1.7.13](#)

### Why the committee made the recommendations

There was no evidence so the committee used their knowledge and experience to make the recommendations.

#### Monitoring (recommendation 1.7.1)

The committee agreed that regular blood monitoring is needed to detect potential abnormalities and inform the baby's care. They agreed that the frequency of blood sampling needs to take into account the clinical stability of the baby, the amount of blood taken, and should also strike a balance between minimising distress to the baby (and parents) and obtaining enough information to guide clinical care. To minimise distress resulting from repeated monitoring, the committee emphasised the need to retrieve as much information as possible from 1 sample, so they recommended combining testing wherever possible and agreeing with the laboratory the best ways to coordinate this. The committee agreed that taking minimal blood volumes would be best for the baby, and that this could be achieved by liaising with the laboratory.

The committee recommended minimum frequencies for monitoring parameters, but they also described situations when increased monitoring may be needed (for example, when there is a change in the composition of parenteral nutrition or when the baby is unstable). They also recommended more frequent monitoring when babies had previous abnormal levels of a particular constituent. However, the committee did not want to be too prescriptive about the level of abnormality or how recently this occurred to allow for a degree of clinical judgement tailored to the needs of each baby.



### **Blood glucose (recommendations 1.7.2 and 1.7.3)**

The committee agreed that glucose should be monitored when starting parenteral nutrition and at every change of the bag, for safety reasons, because the time when a bag is changed would be a critical time where hypoglycaemia or hyperglycaemia could occur. After that, monitoring should depend on the stability of the baby – that is, an unstable glucose level should be monitored more frequently because of the risks associated with hyperglycaemia or hypoglycaemia.

### **Blood pH, potassium, chloride and calcium (recommendations 1.7.4 and 1.7.5)**

The committee agreed that blood pH, potassium, chloride and calcium would usually need to be monitored when starting and when increasing parenteral nutrition. Blood pH is important for a number of reasons, for example, chloride levels cannot be interpreted without knowing the pH, and it is also informative when titrating acetate. Serum sodium is considered in the [section on other constituents of neonatal parenteral nutrition – general principles](#).

### **Serum triglycerides (recommendations 1.7.6 to 1.7.8)**

The committee discussed the variability in monitoring triglycerides in clinical practice, where some neonatal units monitor more or less frequently, and some neonatal units do not monitor triglycerides at all. The committee agreed that recommendations would be useful to improve consistency across clinical practice. They agreed that triglycerides should be monitored when increasing dosages of lipid, because they were aware of evidence that suggests that around 10% of babies do not tolerate recommended intakes of lipids. Monitoring should continue when the maintenance dosage is reached. The committee agreed that when a baby is at risk of hypertriglyceridaemia, for example if the baby is critically ill, triglycerides should be monitored to ensure the safety of the baby.

### **Serum or plasma phosphate (recommendations 1.7.9 and 1.7.10)**

The committee agreed that phosphate would initially require daily monitoring because amino acid intake affects phosphate levels and amino acid intake is changed every day for the first 4 days of parenteral nutrition.

The committee decided that after the maintenance dosage is reached, weekly monitoring would be safe. More frequent monitoring would be needed if there are concerns about

recent abnormal levels or phosphate levels and bone development, and for preterm babies born at less than 32+0 weeks (because preterm babies are at risk of metabolic bone disease of prematurity where their bones become very brittle as a result of insufficient mineralisation).

### **Iron status (recommendation 1.7.11)**

The committee agreed that a number of different factors could affect iron status in babies on parenteral nutrition for longer than 28 days, including the number of transfusions administered as well as the amount of enteral nutrition achieved. It is therefore important to measure ferritin, and iron and transferrin saturations for babies who remain on parenteral nutrition after this time. The committee acknowledged that these measurements should be interpreted with caution in unstable babies because they are acute phase reactants and can be elevated as a result of infective or inflammatory conditions.

### **Liver function (recommendations 1.7.12 and 1.7.13)**

Abnormal liver function tests could indicate the onset of parenteral nutrition-associated liver disease, so the committee agreed it was important to carry out regular liver function tests for babies on parenteral nutrition.

## **How the recommendations might affect practice**

Because there is no current consensus on the monitoring of lipids, these recommendations may change clinical practice. All other recommendations reflect current practice, so the committee agreed there would be no change in practice.

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# **Stopping neonatal parenteral nutrition**

[Recommendations 1.8.1 to 1.8.3](#)

## **Why the committee made the recommendations**

There was some evidence indicating better growth with stopping parenteral nutrition at a

higher volume of enteral feeds (140 ml/kg/day). However, there were some inconsistencies between different studies, so the committee also used their knowledge and experience to make the recommendations. The committee based the ranges on the baby's age because the balance between prioritising nutritional intake and minimising the risk of line sepsis may differ depending on the size of the baby. The committee agreed that there were other factors apart from the volume of enteral feeds that should be considered for all babies before stopping parenteral nutrition (for example, tolerance and amount of enteral feeds delivered as well as the clinical situation).

The lower limit for stopping parenteral nutrition in extremely preterm babies was taken from the evidence, but the upper limit was based on the committee's knowledge and experience. In clinical practice, enteral feeds are not normally fortified at 140 ml/kg/day (as was done in the available evidence), so stopping at this point may risk nutritional deficits, so the committee recommended an upper threshold of 150 ml/kg/day. This may be considered the threshold at which the risks of continuing parenteral nutrition outweigh the benefits. The thresholds for stopping parental nutrition in babies born at or after 28+0 weeks were based on the committee's expertise. The energy stores of older preterm babies and term babies are more replete than those of extremely preterm babies, allowing parenteral nutrition to be stopped at a lower volume.

However, the committee highlighted that stopping parenteral nutrition, even when these ranges are reached, should only be made once the other considerations (in recommendation 1.8.1) have been taken into account.

## **How the recommendations might affect practice**

The committee agreed that the recommendations would reduce variation in clinical practice. For some services, these recommendations may result in a longer duration of parenteral nutrition, which would have associated costs. However, for other services, these recommendations would result in providing parenteral nutrition for a shorter duration and may produce cost savings.

The committee discussed whether the recommendations could result in smaller volumes of parenteral nutrition being prescribed during the transition from parenteral to enteral nutrition, and that these small volumes would not be an efficient use of costs or resources. However, the committee agreed this could be mitigated by giving consideration to residual prescribed volumes of parenteral nutrition when making the decision to stop parenteral nutrition.

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## Service design

[Recommendations 1.9.1 to 1.9.3](#)

### Why the committee made the recommendations

There was some evidence that multidisciplinary team services improve outcomes in newborn babies. However, there were many limitations relating to the evidence, and none of the studies were conducted in the UK. The committee made recommendations that they considered would provide optimum care for babies on parenteral nutrition, using the limited evidence (relating to the clinical role of multidisciplinary teams), and their knowledge of current clinical practice reports in the public domain (particularly related to the team's role in service governance).

The committee acknowledged that inadequacies in the provision of neonatal parenteral nutrition had been highlighted in a 2011 report from the Paediatric Chief Pharmacists Group, *Improving practice and reducing risk in the provision of parenteral nutrition for neonates and children*, which highlighted the need for improvements in practice.

To address these shortcomings and ensure the safety of babies receiving parenteral nutrition, the committee agreed that neonatal parenteral nutrition services should be overseen and supported by a multidisciplinary team with expertise in neonatal parenteral nutrition. The committee specified the membership of the team to ensure that there is expertise in the clinical, prescribing and nutritional core components of neonatal parenteral nutrition (a consultant neonatologist or paediatrician with a special interest in neonatology, as well as a neonatal pharmacist and dietitian). The committee also recognised that access to other roles may be required, such as neonatal nursing, paediatric gastroenterology or expertise in clinical biochemistry to cover specific clinical or specialist areas of parenteral nutrition. The committee listed these different professionals, but agreed that all those listed would not need to see every baby routinely within the unit. The committee decided that an oversight or support team could be available at a local level or within a clinical network to ensure that every unit has access to these professionals when needed.

The committee agreed that enhanced multidisciplinary team input (for assessment and management) may be needed for preterm and term babies with complex needs, for

example, babies with short gut who need parenteral nutrition for long time periods and who therefore have an increased risk of complications. This may involve more frequent meetings between multidisciplinary team members, and may also mean that other specialists are included in the multidisciplinary team, for example, a gastroenterologist. The committee did not want to be prescriptive about which professionals should be in the 'enhanced' multidisciplinary team because this would depend on the needs of each baby.

## **How the recommendations might affect services**

The committee noted that there is currently variation in practice regarding the availability of specialists who are included within multidisciplinary teams, but agreed that these professionals would be available somewhere within a network of care. Arranging and formalising this access may require extra resources. However, babies with complex needs would invariably be seen by professionals from multiple disciplines, so this would not be a change in practice. The recommendations therefore would reduce variation and reinforce current best practice.

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# **Information and support for parents and carers of babies who need neonatal parenteral nutrition**

[Recommendations 1.10.1 to 1.10.4](#)

## **Why the committee made the recommendations**

There was no evidence so the committee used their knowledge and experience to make the recommendations.

Good nutrition underpins good neonatal care, so the committee agreed that giving parents and carers information about parenteral nutrition is important.

The committee recognised that having a baby in a neonatal unit is a challenging and stressful situation, and agreed that the best approach to working with parents and carers is a collaborative one. This should involve giving parents and carers information tailored to their needs, and helping them to feel involved in their baby's care.

The committee noted that principles of good information sharing and communication, as well as encouraging shared decision making, are covered in the [NICE's guideline on patient experience in adult NHS services](#).

Given that there was no evidence, the committee made a recommendation for further research. This is important because having a baby in a neonatal unit can be a stressful and difficult time for parents and carers. Information and support can help parents manage these circumstances and help them feel involved and part of their baby's care, which can improve outcomes. Given that the number of babies needing parenteral nutrition is likely to increase as prematurity survival rates improve, understanding what information and support parents need will help to support good outcomes.

## **How the recommendations might affect practice**

The committee agreed there is variation in practice. These recommendations should improve consistency in how healthcare professionals support parents and carers, and ensure that they are given timely, consistent and appropriate information about parenteral nutrition.

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## Context

Parenteral nutrition refers to intravenous feeding, a technique for providing nutrition to those who are unable to tolerate adequate enteral nutrition (orally or through an enteral tube). It is frequently needed by preterm babies while they establish enteral feeds, critically ill babies, and babies with gastrointestinal disorders who need surgery.

Inadequate nutrition, particularly in preterm babies, can have short-term and long-term health effects, including longer stays in the neonatal unit, an increased risk of infection, and worsened developmental outcomes. There is also evidence that inappropriate nutritional management soon after birth is linked to the development of metabolic syndrome in adults.

Approximately 95,000 babies born in the UK each year need neonatal care (National Neonatal Audit Programme 2016). Parenteral nutrition is widely used in neonatal care. It has become common practice to start it in preterm babies within the first few hours of life, and also to support term babies who are critically ill.

Parenteral nutrition contains nutrients such as glucose, electrolytes, amino acids, lipids, minerals, trace elements and vitamins. It may complement enteral feeding or, in some situations, replace it.

The National Confidential Enquiry into Patient Outcome and Death enquiry into the care of hospital patients receiving parenteral nutrition (2010) reviewed 264 cases of neonatal parenteral nutrition. It found that 73% of cases represented less than 'good practice', 40% had metabolic complications, 40% did not meet nutritional needs, and in 28% the start of parenteral nutrition was delayed. In 37%, the first parenteral nutrition provided was considered inadequate for the patient's needs.

Parenteral nutrition is normally formulated in an aseptic pharmacy unit. It can be in standardised or individualised forms. Prescribing is complex and open to error. Simplified, standardised regimens may reduce this risk, and may reduce costs.

In current practice, virtually all babies born before 31+0 weeks who weigh less than 1.5 kg need parenteral nutrition for a period that depends on gestation, birthweight and other morbidities. Postnatal growth failure is common in babies born before 31+0 weeks. It is associated with an increased need for respiratory support and increased risk of infection.

It is also a risk factor for neurocognitive impairment. Optimal use of parenteral nutrition could potentially avoid postnatal growth failure.

Parenteral nutrition is expensive: for a large tertiary neonatal unit, it costs approximately £175,000 a year.

Given the wide variation in practice, safety concerns and costs, this guideline is needed to ensure that the provision of parenteral nutrition for babies is consistent across units and provides optimal care.



## Finding more information and committee details

To find NICE guidance on related topics, including guidance in development, see the [NICE topic page on postnatal care](#).

For full details of the evidence and the guideline committee's discussions, see the [evidence reviews](#). You can also find information about [how the guideline was developed](#), including [details of the committee](#).

NICE has produced [tools and resources](#) to help you put this guideline into practice. For general help and advice on putting NICE guidelines into practice, see [resources to help you put guidance into practice](#).

# Update information

## Minor changes since publication

**October 2021:** We added links to NICE's guidelines on babies, children and young people's experience of healthcare and on shared decision making in recommendation 1.10.3.

**June 2020:** The range of total energy per gram of amino acid in recommendation 1.5.6 was corrected to '23 to 34 kcal'.

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