BDA The Association of UK Dietitians

Neonatal Dietitians

Affiliated to the Paediatric Specialist Group

The routine supplementation of vitamins and iron and the management of zinc deficiency in preterm and small for gestational age infants

Guidance for Clinical Practice

March 2025

Endorsed by

British Association of Perinatal Medicine

Contents

Glossary

Term	Definition
ALP	Alkaline Phosphatase
BAPM	British Association of Perinatal Medicine
BNFc	British National Formulary for Children
BPD	Bronchopulmonary Dysplasia
CRP	C Reactive Protein
DBM	Donor Breast Milk
DNA	Deoxyribonucleic Acid
EFSA	European Food Safety Agency
ELBW	Extremely Low Birth Weight
ESPGHAN	European Society for Paediatric Gastroenterology Hepatology and Nutrition
GI	Gastrointestinal
IVH	Intraventricular Haemorrhage
kg	Kilogram
LFT	Liver Function Tests
LMPT	Late to Moderate Preterm
MBM	Maternal Breast Milk
NDiG	Neonatal Dietitians Interest Group
PN	Parenteral Nutrition
PPIs	Proton Pump Inhibitors
RBP	Retinol Binding Protein
RCT	Randomized Controlled Trial
ROP	Retinopathy of Prematurity
RNA	Ribonucleic Acid
RNI	Reference Nutrient Intake
VLBW	Very Low Birth Weight
WHEAT	Withholding Enteral Feeds Around Packed Red Cell Transfusion
25 (OH) D	25-hydroxy vitamin D
µg/kg/day	micrograms per kilogram per day
mg/kg/day	milligrams per kilogram per day
IU/kg/day	International Units per kilogram per day
µg/L	micrograms per litre
mg/L	milligrams per litre
µmol/L	micromoles per litre
mL/kg/day	millilitres per kilogram per day

Summary

Vitamin Supplementation

The third trimester of pregnancy is a period of rapid nutrient accretion and the time when fat-soluble vitamin stores are laid down. Premature birth interrupts this process, consequently preterm infants have lower stores of fat-soluble vitamins and potentially higher requirements for all vitamins than those born at term.

This guideline is designed to support appropriate use of nutritional products in settings where supplementation is organisational policy. Recommendations have been formulated through clinical consensus and are based on a thorough literature search, comprising three international publications (1-3) and a detailed quantitative analysis of milk, fortifier and vitamin formulations by gestation and weight, undertaken by the authors (4-12).

Two dosing algorithms for vitamin supplementation have been provided to allow for network/unit preference: Option 1 (dose banding by weight) & Option 2 (single dosing, pragmatic approach) – please choose one.

Iron Supplementation

Preterm and low birth weight infants are at risk of iron deficiency due to low stores at birth, higher requirements due to rapid growth, losses caused by frequent blood sampling, the requirement for parenteral nutrition support for the smallest and sickest infants, which does not routinely contain iron and breast milk does not contain iron (2).

These recommendations have been formulated through clinical consensus. They are based upon a thorough literature search, which includes three international publications (1-3) and a detailed quantitative analysis of milk, fortifier and iron supplementation by gestation and weight, undertaken by the authors (4-12, 13).

Management of Zinc Deficiency

Zinc is an essential trace element, meaning the body is unable to make or store it, requiring continuous dietary intake. Zinc is accrued during the third trimester of pregnancy.

Preterm infants not only have lower reserves and reduced absorption of zinc but will have increased requirements during the postnatal period of rapid growth (66, 67). Zinc deficiency is associated with poor growth, increased risk of infection, skin rash and possible poor neurodevelopment (1, 2). Risk factors for poor zinc status include insufficient zinc intake either via parenteral or enteral route, breastmilk with low zinc levels due to inadequate maternal zinc transfer and excess gastrointestinal losses due to high enterostomy losses >20mL/kg/day or persistent diarrhoea (2, 67).

Recommendations for vitamin supplementation

DaliVit® is not recommended as a first line preparation as it has a much higher vitamin A content than other preparations. Therefore, it is not a directly interchangeable product with others on the market (see Appendix 2).

Option 1: Dose Banding by Weight

Born <34weeks and/or <1.8kg		
Fortified breastmilk (Gold Prem® or Nutriprem®fortifer) **OR** Nutriprem® 1/ Gold Prem® 1	Current weight ≤1kg	0.3mL Abidec®/day
	Current weight >1kg	0.6mL Abidec®/day
Unfortified breastmilk (not recommended *)	Current weight ≤1kg	Abidec® 0.6mL/day (consider Folic Acid 50microgram/day)
	Current weight >1kg	Abidec® 0.6mL/day **and** Colecalciferol 300IU/day (consider Folic Acid 50microgram/day)
On reaching 1.8kg - 2kg ** or discharge ** dependent upon local policy for change to nutrient enriched post discharge formulas		
Fortified breastmilk (Gold Prem®or Nutriprem® fortifier) (including fortified breastmilk feeding post discharge) **OR** Gold Prem® 2/ Nutriprem® 2 **OR** High Calorie Term Formula		Abidec® 0.3mL/day
Unfortified breastmilk		Abidec® 0.6mL/day (consider vitamin K on discharge – see Appendix 1 for dosing)
Term Formula (including specialist term formula)		Abidec® 0.6mL/day
Born 34-36^{+6} weeks and ≥1.8kg		
Breastmilk		400IU/day Colecalciferol (consider vitamin K on discharge – see Appendix 1 for dosing)
Term Formula		400IU/day Colecalciferol

***** ESPGHAN supports the routine use of breast/human milk in infants born <1.8kg**.**

Without breast milk fortifier full nutritional requirements for all electrolytes, vitamins, calcium, phosphate, other minerals and trace elements will not be met.

Consider continuing prescribed supplements for at least 6 months corrected (up to maximum of 1 year actual age), at which point national public health policy on childhood vitamin supplementation should be employed (16,17). Where prescribed on discharge, vitamin K should be continued for a minimum of 3 months (23).

Consider measuring serum 25 (OH) D at 3-4 weeks of life and then every month until discharge (1).

Option 2: Single Dosing, Pragmatic Approach

Born <34weeks and/or <1.8kg	
Fortified breastmilk (Gold Prem® or Nutriprem® fortifer) **OR** Nutriprem® 1/Gold Prem® 1	Abidec® 0.6mL/day
Unfortified breastmilk (not recommended *)	Abidec® 0.6mL/day **and** Colecalciferol 300IU/day (consider Folic Acid 50microgram/day)
On reaching 1.8kg - 2kg ** or discharge ** dependent upon local policy for change to nutrient enriched post discharge formulas	
Fortified breastmilk (Gold Prem® or Nutriprem®fortifier) (including fortified breastmilk feeding post discharge) **OR** Gold Prem® 2/Nutriprem® 2 **OR** Term/Specialist/High Calorie Term Formula	Abidec® 0.6mL/day
Unfortified breastmilk and/or breastfeeding	Abidec® 0.6mL/day (consider vitamin K on discharge – see Appendix 1 for dosing)
Born 34-36^{+6} weeks and ≥1.8kg	
Breastmilk	Abidec® 0.6mL/day (consider vitamin K on discharge – see Appendix 1 for dosing)
Term Formula	Abidec® 0.6mL/day

***** ESPGHAN supports the routine use of breast/human milk in infants born <1.8kg**.**

Without breast milk fortifier full nutritional requirements for all electrolytes, vitamins, calcium, phosphate, other minerals and trace elements will not be met.

Consider continuing prescribed supplements for at least 6 months corrected (up to maximum of 1 year actual age), at which point national public health policy on childhood vitamin supplementation should be employed (16, 17). Where vitamin K prescribed on discharge, vitamin K should be continued for a minimum of 3 months (23).

Consider measuring serum 25 (OH) D at 3-4 weeks of life and then every month until discharge (1).

Recommendations for Iron Supplementation

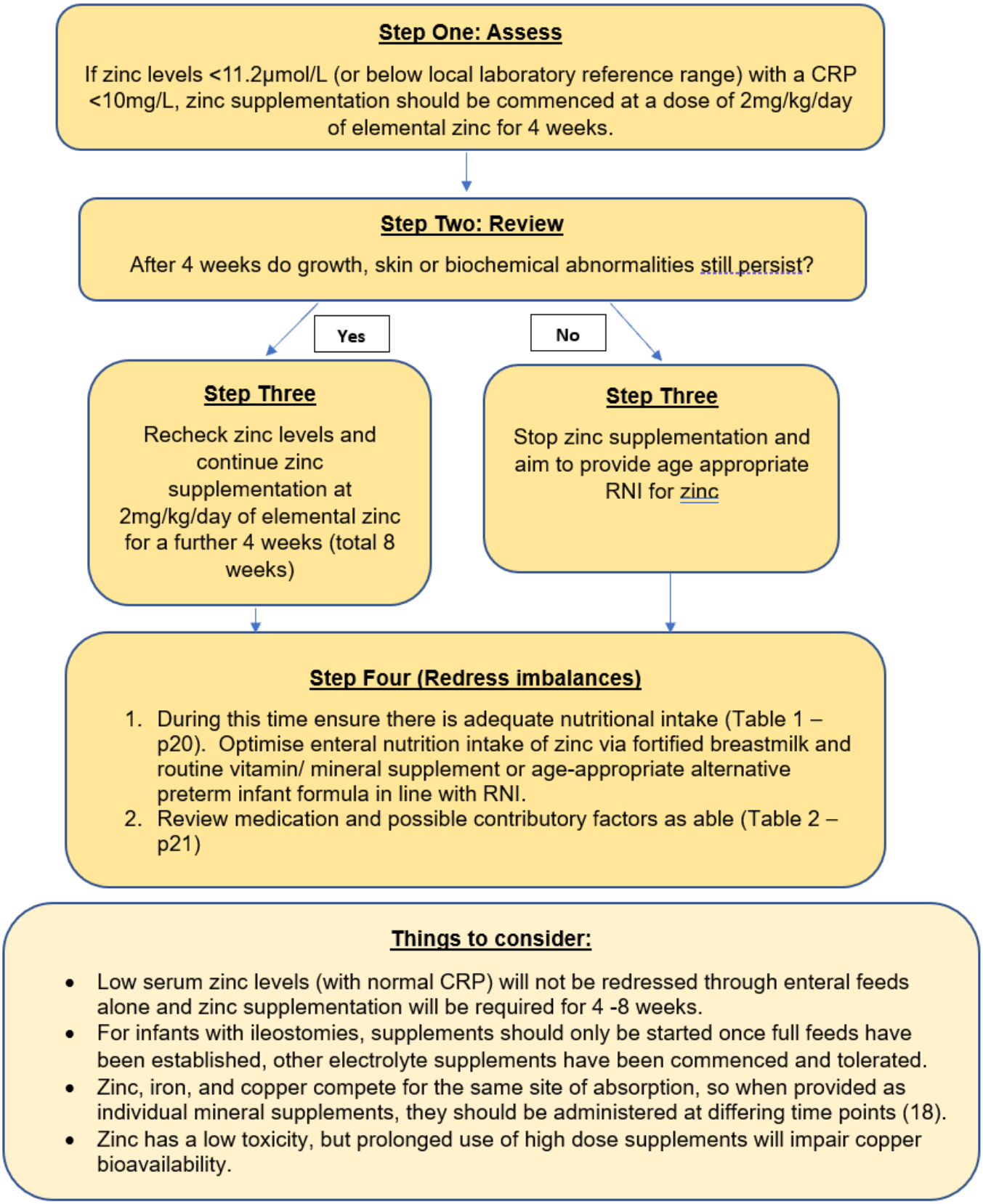
Preterm infant gestation born < 34 weeks and/or birthweight < 1.8 kg (aim 2-3 mg/kg/day) from 2 weeks of age			
Feed	**Working Weight (kg)**	**Sodium feredetate (27.5 mg/5mL) dose (mL/day)**	**Ferrous fumarate* (45mg/5mL) dose (mL/day)**
Breast milk or fortified breast milk with Nutriprem® fortifier	< 1.5	0.5	0.3
	≥ 1.5	1	0.6
Standard or specialist formula designed for term infants	≥ 1	0.5	0.3
Continue supplementation until 12 months actual age**			
The following feeds do not require iron supplementation: Nutriprem 1®, Nutriprem 2®, Gold Prem 1®, Gold Prem 2®, Fortified breast milk with Gold prem® fortifier			

Infant gestation born 34-36^{+6} weeks or >37weeks with a birthweight ≥1.8kg -2.5kg (aim 1-2 mg/kg/day) from 2 weeks of age		
Feed	**Sodium feredetate (27.5 mg/5 mL) dose (mL/day)**	**Ferrous fumarate* (45 mg/5mL) dose (mL/day)**
Breast milk or predominantly breast milk in combination feeding	0.5	0.3
Continue supplementation until 6 months actual age**		
The following feeds do not require iron supplementation: Standard or specialist formula designed for term infants		

* The Galfer® brand of ferrous fumarate has dosing recommendations for preterm neonates from 4 weeks of age. If using other ferrous fumarate products, assess the excipient content prior to use.

** Clinical judgement should be exercised when discontinuing iron supplementation. Some infants may require iron supplementation beyond timeframe stated such as ELBW infants and LMPT infants with birth weight ≤ 2 kilograms.

Recommendations for zinc management in cases of deficiency



Guideline:	Vitamin supplementation in preterm and small for gestational age infants
Version:	1.5
Date:	January 2024 (updated March 2025)
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Approval:	Endorsed by: British Dietetic Association Neonatal Dietitians Interest Group (NDiG) British Association of Perinatal Medicine (BAPM)
Authors:	**Dietitians**: Lynne Radbone RD MBE, Lead Neonatal Dietitian East of England ODN Lynette Forsythe RD, Lead Neonatal Dietitian Northwest ODN Dilyana Kraleva RD, Neonatal Dietitian Nottingham University Hospitals NHS Foundation Trust Katie Hay RD, Lead Neonatal Dietitian East Midlands ODN Rachael Rodley RD, Neonatal Dietitian, Jessop Wing, Sheffield Teaching Hospitals Hester Blair RD, Advanced Dietetic Practitioner (Neonates), Simpsons Centre for Reproductive Health, NHS Lothian **Pharmacist:** Suzannah Hibberd, Neonatal Pharmacist, University Hospital Southampton
Peer Review:	**Dietitians**: Louisa Whitfield-Brown RD, Lead Neonatal Dietitian Northern ODN Stephanie Tagani RD, Clinical Lead Dietitian: Neonates, Imperial College Healthcare NHS Trust Rachel Fox RD, Senior Specialist Dietitian, University Hospitals of Leicester NHS Trust Carol Fudge RD, Childrens Dietitian, Poole General Hospital William Williams RD, Neonatal lead Dietitian. Betsi Cadwaladr University Health Board Sara Clarke RD, Lead Neonatal Dietitian West Midlands ODN and Chair of Neonatal Dietitians Interest Group **Pharmacist:** Melody Chan, Neonatal Pharmacist, University Hospital Southampton **N3 Neonatal Nutrition Network** **Neonatal and Paediatric Pharmacy Group**

1. Introduction

Both fat- and water-soluble vitamins are essential nutrients for whole body function and homeostasis. Water-soluble vitamins are not stored in the body, so need to be provided continuously through dietary provision, whereas fat-soluble vitamins are stored in fatty tissue and the liver. The third trimester of pregnancy is a period of rapid nutrient accretion and the time when fat-soluble vitamin stores are laid down. Premature birth interrupts this process, consequently preterm infants have lower stores of fat-soluble vitamins and potentially higher requirements for all vitamins than those born at term. Although there is some limited evidence for a few key vitamins available from supplementation studies aimed at improving clinical outcomes, an overall lack of studies makes it difficult either to describe the metabolism of vitamins in preterm infants or to determine their vitamin requirements.

Current guidelines for preterm nutritional requirements (1, 2) recognise this lack of evidence and therefore base their recommendations for vitamin intakes on several factors:

- The vitamin dosages used from supplementation studies in preterm infants that demonstrated improvement in clinical outcomes.
- The recommendations of the European Food Safety Authority (EFSA) for term infants (<6 months). Theoretically, the EFSA daily recommendations may underestimate the increased requirements of the rapidly growing preterm infant. However, because of the weight difference between term and preterm infants the authors considered that daily, per kilogram, recommendations for term infants are likely to be adequate for preterm infants as they represent approximately a 3- to 5-fold higher intake per kilogram body weight per day.
- The EFSA best estimate of the vitamin content of mature mother's own milk, when fed at minimal recommended energy intake for a preterm infant of 115Kcal/kg/day.
- The vitamin content of commercial preterm formulas when fed at a volume that provides 115Kcal/kg/day.

2. Scope & evidence

This guideline is designed to support appropriate use of nutritional products in settings where supplementation is organisational policy. Recommendations have been formulated through clinical consensus and are based on a thorough literature search, comprising three international publications (1-3) and a detailed quantitative analysis of milk, fortifier and vitamin formulations by gestation and weight, undertaken by the authors (4-12).

Two dosing algorithms have been provided to allow for network/unit preference:

- Option 1 is a dose banding approach, taking account of an infant's weight. This ensures that intakes of vitamins D and A are largely kept within the upper and lower recommended reference ranges, as per European Society for Paediatric Gastroenterology Hepatology and Nutrition (ESPGHAN) (1) (see table 1 in Appendix 4).
- Option 2 is a single dosing, pragmatic approach and ensures that baseline ESPGHAN requirements are met. In some smaller infants this will provide more than the ESPGHAN recommended daily vitamin A & D intakes (1) (see table 2 in Appendix 4).

Some argue that concerns about potential vitamin A toxicity have led to caution in dosing regimens in preterm infants, which are largely unfounded (19). In one dose comparison study, intramuscular regimens of up to 8500 international units/kg/day (i.e. in a 0.5kg infant) were administered and potential adverse effects were seen in less than 5% (20). However, ESPGHAN (1) acknowledge that there is insufficient data to change the current recommendation for vitamin A in preterm infants.

This guideline is to be used as an adjunct to clinical decision making. Where infants are receiving volumes of milk considered outside the “usual” range of 150 -165mL/kg/day, advice should be sought from a neonatal dietitian.

3. Supply & alternatives

A limited range of suitable multivitamin preparations are available for use in the preterm population (Appendix 2). It is widely recognised that intermittent supply issues of first line vitamin preparations bring difficulties in provision to infants. A table of alternative products suitable for use during these periods, or where peanut and soya avoidance is prudent, can be found in Appendix 3.

	ESPGHAN (2022)
Thiamine (B1) (micrograms/kg/day)	140-290
Pantothenic acid (B5) (mg/kg/day)	0.6-2.2
Biotin (B7) (micrograms/kg/day)	3.5-15
Niacin (B3) (micrograms/kg/day)	1100-5700
Vitamin C (Ascorbic acid) (mg/kg/day)	17-43
Riboflavin (B2) (micrograms/kg/day)	200-430
Pyridoxine (B6) (micrograms/kg/day)	70-290
Folic acid (B9) (micrograms/kg/day)	23-100
Cobalamin (B12) (micrograms/kg/day)	0.1-0.6
Vitamin A (Retinol) (international units/kg/day)	1333-3300 (400-1000micrograms retinol ester/kg/day)
Vitamin D (Colecalciferol) (international units/kg/day)	400-700 international units/kg/day (<1000 international units/day)
Vitamin E (Alpha-tocopherol) (mg/kg/day)	2.2 – 11
Vitamin K (Phytomenadione) (micrograms/kg/day)	4.4 – 28

4. Preterm vitamin requirements

Recommended enteral intakes for vitamins (ESPGHAN) (1)

5. Who should receive vitamin supplementation?

The gestation below which additional vitamins are required is unclear, consequently supplementation practice has, in the past, varied across the UK.

Current guidelines provide recommendations for vitamin intakes in extremely low birth weight (ELBW) and very low birth weight (VLBW) infants (2) and for infants <1800g (1) but neither make any delineation by degree of prematurity.

The vitamin requirements of late and moderate preterm (LMPT) infants, defined as infants born 32+0 – 33+6 weeks gestation (moderate preterm) and 34+0 – 36+6 weeks gestation (late preterm), are likely to be higher than those for term infants, but again, there are insufficient data to inform intake levels for any except for vitamin D. Current recommendations are to provide all LMPT infants with a vitamin D supplement from birth and throughout early childhood (21, 22).

Due to the lack of detailed guidance, a pragmatic approach needs to be taken as to the population this guideline applies to however, available evidence would suggest vitamin supplementation (in particular, vitamin D) is required for all infants born <37 weeks gestation.

Lack of robust evidence regarding folate supplementation has led to variation in practice. Dosing advice for organisations choosing supplementation is contained in the following tables. The same applies to vitamin K. Evidence, products and dosing advice for organisations adopting supplementation of all infants <37 weeks & exclusively fed human milk for ≥ 3 months post discharge

are discussed in the appendices of this guideline (23).**6. Recommendations for vitamin supplementation**

DaliVit® is not recommended as a first line preparation as it has a much higher vitamin A content than other preparations. Therefore, it is not a directly interchangeable product with others on the market (see Appendix 2).

Option 1: Dose Banding by Weight

Born <34weeks and/or <1.8kg		
Fortified breastmilk (Gold Prem® or Nutriprem®fortifer) **OR** Nutriprem® 1/ Gold Prem® 1	Current weight ≤1kg	0.3mL Abidec®/day
	Current weight >1kg	0.6mL Abidec®/day
Unfortified breastmilk (not recommended *)	Current weight ≤1kg	Abidec® 0.6mL/day (consider Folic Acid 50microgram/day)
	Current weight >1kg	Abidec® 0.6mL/day **and** Colecalciferol 300IU/day (consider Folic Acid 50microgram/day)
On reaching 1.8kg - 2kg ** or discharge ** dependent upon local policy for change to nutrient enriched post discharge formulas		
Fortified breastmilk (Gold Prem®or Nutriprem® fortifier) (including fortified breastmilk feeding post discharge) **OR** Gold Prem® 2/ Nutriprem® 2 **OR** High Calorie Term Formula		Abidec® 0.3mL/day
Unfortified breastmilk		Abidec® 0.6mL/day (consider vitamin K on discharge – see Appendix 1 for dosing)
Term Formula (including specialist term formula)		Abidec® 0.6mL/day
Born 34-36^{+6} weeks and ≥1.8kg		
Breastmilk		400IU/day Colecalciferol (consider vitamin K on discharge – see Appendix 1 for dosing)
Term Formula		400IU/day Colecalciferol

***** ESPGHAN supports the routine use of breast/human milk in infants born <1.8kg**.**

Without breast milk fortifier full nutritional requirements for all electrolytes, vitamins, calcium, phosphate, other minerals and trace elements will not be met.

Consider continuing prescribed supplements for at least 6 months corrected (up to maximum of 1 year actual age), at which point national public health policy on childhood vitamin supplementation should be employed (16, 17). Where vitamin K prescribed on discharge, vitamin K should be continued for a minimum of 3 months (23).

Consider measuring serum 25 (OH) D at 3-4 weeks of life and then every month until discharge (1).

Option 2: Single Dosing, Pragmatic Approach

Born <34weeks and/or <1.8kg	
Fortified breastmilk (Gold Prem® or Nutriprem® fortifer) **OR** Nutriprem® 1/Gold Prem® 1	Abidec® 0.6mL/day
Unfortified breastmilk (not recommended *)	Abidec® 0.6mL/day **and** Colecalciferol 300IU/day (consider Folic Acid 50microgram/day)
On reaching 1.8kg - 2kg ** or discharge ** dependent upon local policy for change to nutrient enriched post discharge formulas	
Fortified breastmilk (Gold Prem® or Nutriprem®fortifier) (including fortified breastmilk feeding post discharge) **OR** Gold Prem® 2/Nutriprem® 2 **OR** Term/Specialist/High Calorie Term Formula	Abidec® 0.6mL/day
Unfortified breastmilk and/or breastfeeding	Abidec® 0.6mL/day (consider vitamin K on discharge – see Appendix 1 for dosing)
Born 34-36^{+6} weeks and ≥1.8kg	
Breastmilk	Abidec® 0.6mL/day (consider vitamin K on discharge – see Appendix 1 for dosing)
Term Formula	Abidec® 0.6mL/day

Consider continuing prescribed supplements for at least 6 months corrected (up to maximum of 1 year actual age), at which point national public health policy on childhood vitamin supplementation should be employed (16, 17). Where vitamin K prescribed on discharge, vitamin K should be continued for a minimum of 3 months (23).

***** ESPGHAN supports the routine use of breast/human milk in infants born <1.8kg**.**

Without breast milk fortifier full nutritional requirements for all electrolytes, vitamins, calcium, phosphate, other minerals and trace elements will not be met.

Consider measuring serum 25 (OH) D at 3-4 weeks of life and then every month until discharge (1).

Guideline:	Iron supplementation in preterm and small for gestational age infants
Version:	1.5
Date:	January 2024 (amended March 2025)
Review Date:	October 2027 by ODN's Dietetic Group (NatNeoRD) and Affiliates
Approval:	Endorsed by: Neonatal Dietitians Interest Group (British Dietetic Association)
Authors:	**Dietitians**: Louisa Whitfield-Brown RD, Lead Neonatal Dietitian Northern ODN Stephanie Tagani RD, Clinical Lead Dietitian: Neonates, Imperial College Healthcare NHS Trust Rachel Fox RD, Senior Specialist Dietitian, University Hospitals of Leicester NHS Trust Carol Fudge RD, Childrens Dietitian, Poole General Hospital William Williams RD, Neonatal lead Dietitian. Betsi Cadwaladr University Health Board **Pharmacist:** Melody Chan, Neonatal Pharmacist, University Hospital Southampton
Peer Review:	**Dietitians:** Lynne Radbone RD MBE, Lead Neonatal Dietitian East of England ODN Lynette Forsythe RD, Lead Neonatal Dietitian Northwest ODN Dilyana Kraleva RD, Neonatal Dietitian Nottingham University Hospitals NHS Foundation Trust Katie Hay RD, Lead Neonatal Dietitian East Midlands ODN Rachael Rodley RD, Neonatal Dietitian, Jessop Wing, Sheffield Teaching Hospitals Hester Blair RD, Advanced Dietetic Practitioner (Neonates), Simpsons Centre for Reproductive Health, NHS Lothian Sara Clarke RD, Lead Neonatal Dietitian West Midlands ODN and Chair of Neonatal Dietitians Interest Group **Pharmacist:** Suzannah Hibberd, Neonatal Pharmacist, University Hospital Southampton **N3 Neonatal Nutrition Network** **Neonatal and Paediatric Pharmacy Group**

1. Introduction

Iron is an essential micromineral which is required for heme synthesis, oxygen transport, enzyme functions and brain development (2).

Preterm and low birth weight infants are at risk of deficiency due to low stores at birth, higher requirements due to rapid growth, losses caused by frequent blood sampling and the requirement for parenteral nutrition support for the smallest and sickest infants, which does not routinely contain iron (2). Maternal breast milk is recognised as the optimal feed for preterm infants (3). However, maternal breastmilk does not meet the elevated iron requirements of preterm infants.

Iron deficiency anaemia should be avoided as it may adversely affect brain development (2). Excessive intakes of iron can also be detrimental to preterm infants and should be avoided, as there is no mechanism for excretion. Excess iron may increase oxidative stress and associated complications of prematurity (2).

Current guidelines for preterm nutritional requirements (1, 2) recommend intakes that will not be met by maternal breast milk (and some commercial feeds used when maternal breast milk is unavailable). Iron supplementation is therefore recommended (1, 3). The iron supplement used in the United Kingdom is sodium feredetate 27.5mg of iron per 5mL oral solution and the guidance in this document is based on this formulation.

2. Scope & evidence

These recommendations have been formulated through clinical consensus. They are based upon a thorough literature search, which includes 3 international publications (1-3) and a detailed quantitative analysis of milk, fortifier and iron supplement by gestation and weight, undertaken by the authors (4-12, 13).

A pragmatic approach has been taken to ensure that baseline requirements, as detailed by the European Society for Paediatric Gastroenterology Hepatology and Nutrition (ESPGHAN) (1) are met, and that where intakes higher than the upper range are suggested, they do not exceed levels which could be considered harmful (e.g. toxicity).

This guideline is to be used as an adjunct to clinical decision making. Where infants are receiving volumes of milk considered outside the “usual” range of 150 -165mL/kg/day advice should be sought from a suitably experienced neonatal dietitian.

3. Preterm and small for gestational requirements

Current guidelines provide recommendations for iron intakes for any infants born <1.8kg (1), preterm infants born <1.5kg, 1.5-2kg, 2-2.5kg (2, 21) and term infants born <2.5kg (3).

To meet these requirements exactly using sodium feredetate 27.5mg of iron per 5mL oral solution would involve multiple different doses based on gestation and weight. The group felt multiple doses and different ages at which supplementation commenced would lead to non-compliance so a pragmatic approach to dosing was taken. The dose of iron given in mixed feeding regimens should be informed by the predominant feed (that is the feed which comprises over 50% of intake).

Where recommendations regarding commencement of iron supplements are made, they are not uniform or may suggest a staggered approach. The group have taken a pragmatic view and recommend iron supplementation from 2 weeks of age to guard against omission.

The guidelines recommend iron supplementation until adequate iron intake from intake of solids. There is inadequate neonatal dietetic resource nationally to provide the individual assessment required to support this. Giving iron supplements to 12 months corrected age would minimise risk

of anaemia in the ELBW and VLBW infants. However, the group took a pragmatic approach and recommended discontinuing iron supplementation at 12 months actual age. Clinical judgement should be exercised where there is developmental delay or feeding difficulties.

A summary of guidance from the international guidelines and studies (1-3, 21) focusing on iron supplementation is detailed the table below:

Guideline	Weight (kg)	Amount (expressed as elemental iron)	Start	End
ESPGHAN 2022 (1)	<1.8 ≥1.8	2-3mg/kg Not specified	2 weeks Not specified	6-12 months Not specified
Koletzko 2021 (2)	<1.5 1.5 - 2 2 – 2.5	2-3mg/kg 2mg/kg 1-2mg/kg	2 weeks 2-4 weeks 4-6 weeks	6-12 months 6-12 months 6 months
BAPM 2023 – Late to moderate preterm infants (21)	<2 <2.5	2-3mg/kg 1-2mg/kg	Not specified	At least 6 months
WHO 2022 – term infants (3)	<2.5	2-4mg/kg	When enteral feeds are well established	Until baby receives iron from another source

4. Recommendations for iron supplementation

Dosing preterm infant gestation born < 34 weeks and/or birthweight < 1.8 kg (aim 2-3 mg/kg/day) from 2 weeks of age

Feed	Working Weight (kg)	Sodium feredetate (27.5 mg/5mL) dose (mL/ day)	Ferrous fumarate * (45mg/5mL) dose (mL/day)
Breast milk or fortified breast milk with Nutriprem® fortifier	< 1.5	0.5	0.3
	≥ 1.5	1	0.6
Standard or specialist formula designed for term infants	≥ 1	0.5	0.3
Continue supplementation until 12 months actual age**			
The following feeds do not require iron supplementation: Nutriprem 1®, Nutriprem 2®, Gold Prem 1®, Gold Prem 2®, Fortified breast milk with Gold prem® fortifier			

Infant gestation born 34-36^{+6} weeks or >37weeks with a birthweight ≥1.8kg -2.5kg (aim 1-2 mg/kg/day) from 2 weeks of age

Feed	Sodium feredetate (27.5 mg/5 mL) dose (mL/day)	Ferrous fumarate* (45 mg/5 mL) dose (mL/day)

Breast milk or predominantly breast milk in combination feeding	0.5	0.3
Continue supplementation until 6 months actual age**		
The following feeds do not require iron supplementation: Standard or specialist formula designed for term infants		

* The Galfer® brand of ferrous fumarate has dosing recommendations for preterm neonates from 4 weeks of age. If using other ferrous fumarate products, assess the excipient content prior to use (61).

** Clinical judgement should be exercised when discontinuing iron supplementation. Some infants may require iron supplementation beyond timeframe stated such as ELBW infants and LMPT infants with birth weight ≤ 2 kilograms.

5. Monitoring supplementation

Ferritin is used as a marker of iron status, with < 35-40microgram/L indicating deficiency and >300-350microgram/L signifying iron overload (1). Where inflammation or infection are evident, serum ferritin should not be used as marker as it will be elevated (1). Serum ferritin is not a reliable marker where liver disease is present (1).

It is recognised the individual iron status of ELBW and VLBW infants will vary, and repeated measurements of ferritin are recommended by international guidance (1). Phlebotomy contributes to the risk of iron deficiency. Clinical judgement should be exercised in terms of when and how often ferritin is tested in this patient group. Risk of iron deficiency, reliability of ferritin as a marker (based on clinical condition of the infant) and minimising painful stimuli should all be considered. Iron deficiency and anaemia have been observed in VLBW infants in the first year of life. Compliance with iron supplementation post discharge should be encouraged (49).

Increasing iron dose to 3-4mg/kg/day (in some cases 6 mg/kg/day) should be considered if ferritin < 35-70microgram/L, but an intake of >3mg/kg/day for more than a few weeks should be avoided due to risk of adverse effects (1). Infants receiving erythropoietin treatment may require higher doses of iron, up to 6mg/kg/day (1). If ferritin > 300microgram/L (in the absence of inflammation or liver disease) iron supplementation should be stopped (1), and Nutriprem® breast milk fortifier (which is not fortified with iron) should replace Gold Prem® Breast Milk Fortifier (a source of iron), until serum ferritin falls below this level.

6. Iron supplementation and blood transfusion

Iron supplementation following blood transfusion

There is currently limited guidance on whether iron supplementation should be withheld post blood transfusion. This is due to limited research conducted in this area. Iron supplementation should be withheld following blood transfusions in preterm babies where ferritin levels are >300 microgram/L or for babies with haemolytic disorders as these may predispose the infant to iron overload. Iron should be restarted when ferritin falls below 300microgram/L (2). There is no clear guidance on when to recheck ferritin, so discussion locally is required. If there is infection or inflammation, ferritin will be elevated and use of ferritin as a marker of iron status should be postponed (2). In cases where babies are transfused for the anaemia of phlebotomy losses or external haemorrhage, it may be appropriate to continue iron supplementation (50).

Enteral feeding and transfusions

There is currently insufficient evidence from randomised controlled trials to guide whether feeds should be stopped during transfusion (51). Some studies suggest that feeding during transfusion increases morbidity and mortality (52), whilst others show no difference with or without feeds during transfusion (53).

It is hoped that the WHEAT trial (Withholding Enteral feeds Around packed red cell Transfusion) may provide more evidence for practice in this area. This is an ongoing multi-centre, randomised point of care trial aiming to find out whether withholding milk feeds before, during, and after blood transfusion in preterm infants reduces the risk of necrotising enterocolitis (54).

7. Considerations when administering iron supplements

In general, it is advised to give iron supplements on an empty stomach, and apart from food, to maximise absorption of iron. However, there is a historical consensus that the osmolality of enteral feeds should not exceed 450mOsm/kg (62). The physiological response to hyperosmolar solutions is delayed gastric emptying (62) so it may be prudent to dilute iron supplements in milk feeds prior to administration (62). Srinivasan et al. (2009) recommend every 0.1mL of Sodium Feredetate needs a milk volume of 1.2mL (63). Some centres choose to give the iron supplement just before a milk feed to ensure the full dose is taken and ensure the iron supplement is mixed with feed to maximise tolerance.

Guideline:	Management of zinc deficiency in preterm and small for gestational age infants
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Approval:	Endorsed by: Neonatal Dietitians Interest Group (British Dietetic Association)
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1. Introduction

Zinc is an essential trace element, meaning the body is unable to make or store it, requiring continuous dietary intake. Zinc is accrued during the third trimester of pregnancy (14). It is one of the most prevalent trace elements in the brain and contributes to its structure and function (64). It has an important role in gene transcription, immune defence (65), growth due to its central role in the production of enzymes integral to the production of DNA and RNA (64) and tissue differentiation (2).

Preterm infants not only have lower reserves and reduced absorption of zinc but will have increased requirements during the postnatal period of rapid growth (66, 67). Zinc deficiency is associated with poor growth, increased risk of infection, skin rash and possible poor neurodevelopment (1, 2). Risk factors for poor zinc status include insufficient zinc intake either via parenteral or enteral route, breastmilk with low zinc levels due to inadequate maternal zinc transfer and excess gastrointestinal losses due to high enterostomy losses >20mL/kg/day or persistent diarrhoea (2, 67). Genetic defects in zinc transporters located in the mammary gland can lead to breastmilk containing no zinc leading to cases of acrodermatitis in the neonatal period secondary to zinc deficiency (70). Zinc excretion is also affected by renal immaturity, and concomitant use of medication such as diuretics and steroids (67, 71).

Zinc does not have a pro-oxidant effect, and adverse effects of excess zinc intakes are rarely reported, although copper absorption may be impacted with high zinc intakes over a long period time i.e., > 3months (2).

2. Scope & evidence

These recommendations have been formulated through clinical consensus. They are based upon a thorough literature search, which includes international publications (1,2).

3. Preterm and small for gestational requirements

Recommended nutrient intakes (RNI) for zinc have been established (Table 1). It should be noted the recommended nutrient intakes (RNI) intake should not be used to treat deficient states, as therapeutic supplementation will be required for a short period of time to treat deficiency. Current guidelines recommend an enteral zinc intake of 2-3mg/kg/day for preterm infants < 1.8kg (1, 2).

There are no specific recommendations for small for gestational age or late to moderate preterm infants. However, there are recommended nutrient intakes for zinc for infants and children, which would include late preterm infants and small for gestational age infants (18).

Guideline	Age range/weight	Recommended intake (Parenteral RNI)	Recommended intake (Enteral RNI)
ESPGHAN 2022 (1)	<1.8kg	400-500 micrograms/kg/day	2-3 mg/kg/day
Koletzko 2021 (2)	<1.8kg	400-500 micrograms/kg/day	2-3 mg/kg/day
Department of Health 1991 (18)	0-6 months post term		4 mg/kg/day
Department of Health 1991 (18)	7-12 months post term		5 mg/kg/day
ESPGHAN 2018 (15)	0-6 months post term	250 micrograms/kg/day	
ESPGHAN 2018 (15)	7-12 months post term	100 micrograms/kg/day	

Table 1: Recommended nutrient intake (RNI) for zinc in nutrition support

4. Optimising zinc intakes and treating deficiency

Zinc is an essential element for weight gain and linear growth. There are several contributing factors associated with low zinc levels, including enterostomy losses and use of certain medication (Table 2).

Zinc deficiency can be prevented by ensuring sufficient zinc is provided in nutrition support (parenteral nutrition and enteral) to meet recommended nutrient intakes. This is especially important where there is a high protein intake as more zinc will be required to support linear growth and muscle mass accretion (66). The NDiG group and others (Cochrane (65) and ESPGHAN (1)) found no evidence to support routine zinc supplementation over and above the recommended nutrient intake. Cases of zinc toxicity are rare but excessive prolonged zinc supplementation over months can also lead to copper and iron deficiency (65).

Table 2	Causes of abnormal biochemistry	Action
PN > 21 days	Limitation of zinc in PN	Where able increase enteral intake of full fortified breast milk
Unfortified breast milk	Unfortified breast milk does not contain adequate zinc	Infants <1.8kg at birth need fully fortified breast milk or preterm infant formula
Enterostomy losses	High small bowel ostomy losses ≥20mL/kg/day is associated with increased zinc losses	Review factors associated with ostomy losses, aiming to control output to <20mL/kg/day
Systemic Glucocorticoids	Reduce gut absorption of minerals including zinc which is essential for bone growth	Monitor growth and check zinc levels as per guideline
Proton pump inhibitors	Reduced gut absorption of zinc (neutralisation of stomach acid)	Refer local guidelines regarding the management of reflux
Diuretics	Increased urinary zinc losses	Encourage regular review of ongoing diuretic use with consultant and ensure on lowest effective dose

Table 2: Contributory factors in zinc insufficiency and recommended actions

5. Recommendations for Zinc Screening

ESPGHAN recommend serum zinc levels should be measured in infants on long term parenteral nutrition (PN) at day 28 life and in the absence of ongoing inflammatory response. Other infants at high risk of zinc deficiency, may include those:

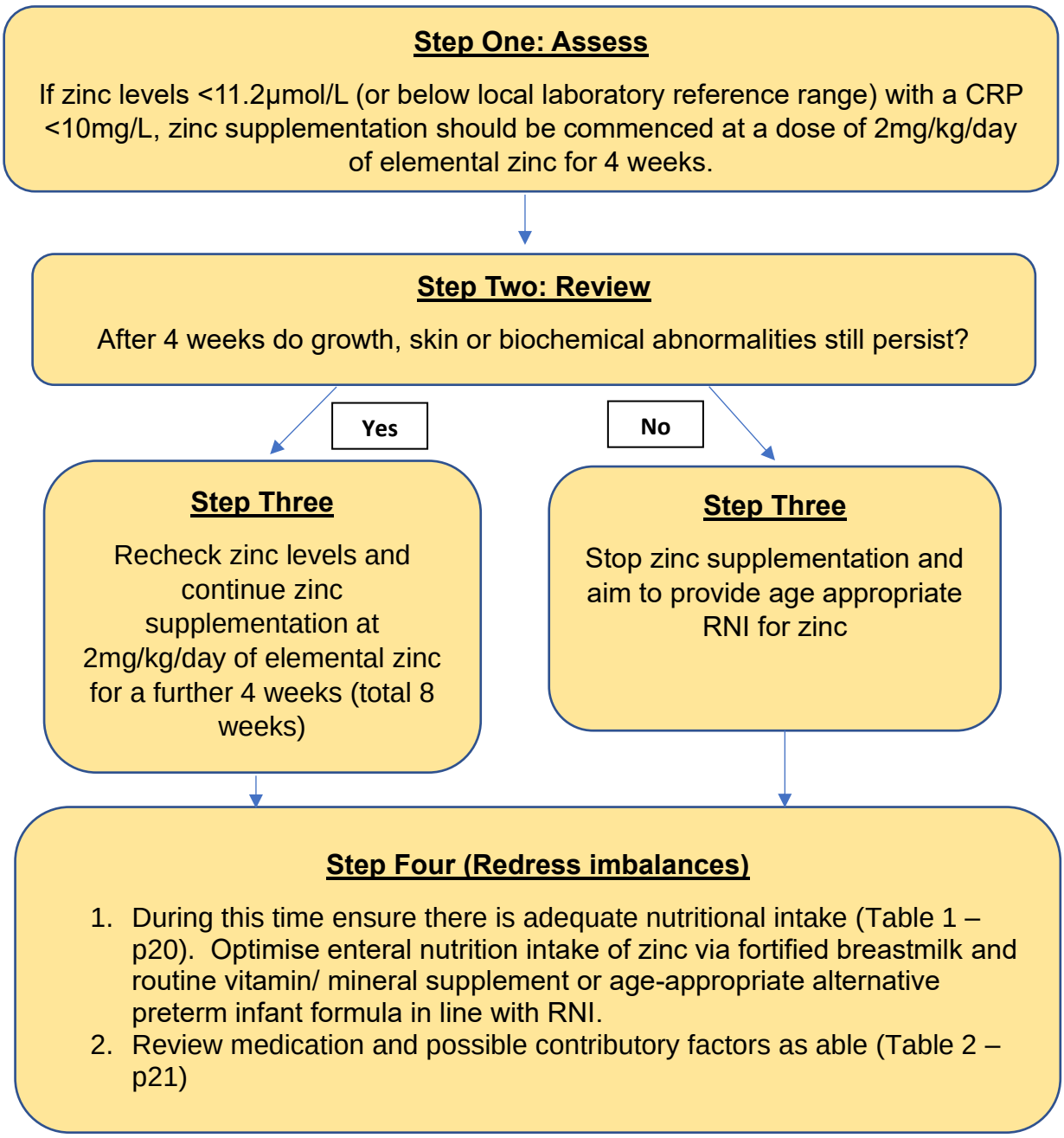
- On PN at day 21 of life
- Born ≤1kg or ≤28 weeks gestation
- With acrodermatitis enteropathica
- Achieving poor growth (length)
- Where ALP is below local reference range (or ≤61 unit/L)
- With persistent GI fluid losses following enterostomy ≥20mL/kg/day

Where zinc deficiency is identified (<11.2µmmol/l) and a CRP ≤10mg/l, oral elemental zinc of 2mg/kg for a period of 4 weeks should be provided. Where oral supplementation is not possible in PN dependent infants, additional intravenous zinc should be considered (1, 2)

Please note:

1. Refer to your local laboratory for blood tube guidance. Note some tubes contain an orange/black rubber ring in the top, which may contain zinc and will affect the accuracy of the reading.
2. When completing a serum zinc measurement, it is important that routine bloods of liver function test (LFT) and C-reactive protein are completed at the same time.
3. CRP levels reflect an acute inflammatory response. Serum zinc levels may be falsely low if CRP >10mg/L. Serum zinc measurements should only be completed when CRP <10mg/L.

6. Recommendations for zinc management in cases of deficiency



Things to consider:

- Low serum zinc levels (with normal CRP) will not be redressed through enteral feeds alone and zinc supplementation will be required for 4 -8 weeks.
- For infants with ileostomies, supplements should only be started once full feeds have been established, other electrolyte supplements have been commenced and tolerated.
- Zinc, iron, and copper compete for the same site of absorption, so when provided as individual mineral supplements, they should be administered at differing time points (67).
- Zinc has a low toxicity, but prolonged use of high dose supplements will impair copper bioavailability.

Solvazinc®, AadZinc® and Aactizinc®. Dosing in this guideline is based on Solvazinc® (68). The BNFc specifically states that 125mg of zinc sulfate monohydrate is equivalent to 45mg of elemental zinc in Solvazinc®. This product has gone through the licensing process and is a recognised "Pharmacy Only Medicine" (68). Contact local pharmacist for preparation and administration guidance.

The group suggest a dose of 2mg/kg/day for preterm babies (69, 71). This is higher than the BNFc dosage of 1mg/kg/day which just refers to neonates. Preterm babies will not have the stores of zinc that term babies are born with and have higher urinary losses (67) and therefore, if deficient, they will most likely need more zinc to correct the deficiency.

Administration of Solvazinc® Effervescent tablets

1. Dissolve one tablet (containing 45mg elemental zinc) in 8.4ml of water (each tablet displaces approximately 0.6ml of water and so the final concentration obtained will be approximately 5mg/ml).
2. Once the tablet has fully dispersed and fizzing has stopped, which is usually after about 5 minutes, use the necessary volume of 5mg/ml solution to administer the dose required.
3. Discard the remaining solution.

Supplementary Information

Using licensed medicines, unlicensed medicines and food supplements

Wherever possible, licensed medications should be used for treating patients. These medicines will have a product license (PL) number on the packaging indicating they undergone full evaluation by the MHRA (72).

Unlicensed medicines don't have a UK Marketing authorisation but meet the definition of a medicine in that they have properties for treating or preventing disease or are used for correcting, restoring or modifying a physiological, metabolic or immunological function. Pharmacists and prescribers must assure themselves of the quality, safety and efficacy of the unlicensed medicine they want to use (73).

Food supplements are defined as "a concentrated source of a vitamin or mineral or other substance with a nutritional or physiological effect, alone or in combination and is sold in dose form." (74). Food supplements are made to different quality standards to medicines and are not evaluated by the MHRA. It is not possible to gain additional assurances from the manufacturers of food supplements.

Within this guidance there is reference to products that are considered to be food supplements such as certain brands of zinc, iron and phytomenadione. Where possible a licensed medication should be selected over a food supplement and a risk assessment should be completed if a food supplement is used over a licensed product.

Excipients

When choosing a product to use in children, do consider the products excipients. For further information see https://nppg.org.uk/choosing-an-oral-liquid-for-a-child/ which contains information on assessing excipient content.

Appendices

Appendix 1

Evidence to Support Vitamin Recommendations

Water Soluble Vitamins (including Folic Acid)

Water soluble vitamins are essential nutrients for whole body function and homeostasis. For most of the water-soluble vitamins there are very little data to provide evidence based dietary recommendations for preterm infants. In the absence of robust evidence recommendations are often inflated to ensure adequacy is well in excess. Current recommendations for water soluble vitamins predominantly reflect the amounts added from industry in preterm infant formulas. It is recommended to monitor nutrient status of preterm infants fed unfortified human breastmilk. Intakes above dietary recommendations are unlikely to be of benefit in improving patients' outcomes (2).

Folate is essential to form normal red blood cells and certain amino acids. In one study folate intake has a positive association with weight and length gain in extreme preterm infants (24). Plasma folate is lower in infants receiving only human breast milk rather than fortified human milk or preterm infant formula. Studies have shown no evidence of folate deficiency in infants receiving preterm formula or breast milk fortifiers suggesting adequate intake. Markers used in these studies were serum concentrations or haematological profile results (25) including raised levels of homocysteine (a biomarker of folate deficiency) (26). Milk formulas and breast milk fortifiers usually contain much higher amounts of folate than breast milk. Folic acid is not present in standard vitamin supplements so needs to be supplemented separately.

Fat Soluble Vitamins

Vitamin D (Calciferol)

Vitamin D, a fat-soluble vitamin, is essential for the absorption of calcium and phosphorus and is therefore vital in bone formation. Supplementation is of no benefit to bone health if there are inadequate supplies of these two minerals, though its exact mechanism is unknown. Further study is needed to identify preterm vitamin D physiology, and the status required to be most protective of bone and extra skeletal development (2).

Vitamin D is primarily transferred to the foetus in the third trimester of pregnancy and is also impacted by the mother's vitamin D status (2). Consequently, many preterm infants have low vitamin D levels at birth (27, 28). There is no consensus regarding the definition of vitamin D deficiency in infants. ESPGHAN guidance pragmatically suggest that a serum 25-hydroxy vitamin D concentration >50nmol/L be used to indicate sufficiency, but that concentrations >120nmol/L be avoided (1).

There are few adequately powered controlled trials on which to base firm recommendations for dosing and duration of vitamin D supplementation in preterm infants. ESPGHAN identified studies with dosage ranges of 200-300IU/kg/day to 400-670IU/kg/day that sufficiently reduced vitamin D deficiency and suggest a dosing regimen of 400-700IU/kg/day (<1000IU/kg/day) (1).

Several studies have also investigated the safety of vitamin D supplementation. They have identified toxicity in some, particularly very low birthweight infants, on a variety of standard dosing regimens (not calculated per kg bodyweight) and which were implemented without regular blood monitoring of vitamin D status (29 - 31). Supplementation with excess active vitamin D may cause calcium resorption of the bone and renal disease (e.g. nephrocalcinosis) and should only be considered where there is clear biochemical deficiency or poor absorption (e.g. significant cholestatic liver disease). ESPGHAN (1) recommends measuring serum 25 (OH) D at 3-4 weeks of life and then every month until discharge.

Vitamin A (Retinol)

Vitamin A is a fat-soluble vitamin that is essential for growth, body regulation and differentiation of cells, including the retina of the eye and lung maturation. Preterm infants are born with low plasma concentration of retinol and retinol binding protein (RBP) (32). They are also susceptible to vitamin A deficiency due to low transplacental transport, poor enteral nutrition post birth and reduced gastrointestinal absorption (32).

Recent Cochrane reviews (2016) showed that additional vitamin A supplementation in premature infants may reduce the risk of mortality and chronic lung disease as well as lower the incidence of retinopathy of prematurity (34, 35). However, those studies investigated intramuscular injections and their effect on bronchopulmonary dysplasia (BPD) and have been found to be painful, therefore it is not common practice. The evidence of the beneficial effects of enteral vitamin A supplementation at higher doses is inconsistent.

Recommended daily intake of vitamin A for premature infants on the neonatal unit is 1333-3300 IU/kg/day (400-1000microgram retinol ester/kg/day). However, according to the most recent ESPGHAN guidelines (2022), higher intake of vitamin A may be required for those infants with hepatic impairment and lower doses of vitamin A for those with renal impairment (1).

Vitamin E (Tocopherol)

Vitamin E encompasses a group of biologically active tocopherols (1). This nutrient functions as an important antioxidant supporting the prevention of haemolytic anaemia, BPD and retinopathy of prematurity (ROP) (36). In addition, it may play a role in stimulating immunity (36) and protecting against intraventricular haemorrhage (IVH) however there is evidence that it may also increase the risk of sepsis (37). Low circulating levels of vitamin E are noted in preterm infants at birth (38). Milk from mothers who delivered preterm however can contain a higher vitamin E content as does preterm formula in comparison to term formula. Studies of routine enteral vitamin E supplementation in this group suggest maintaining plasma vitamin E concentrations of 10–35mg/L (Minimum dose of 3.8mg/kg/day) (1). No clinical benefits have been seen however, and the recommended daily intake of vitamin E in preterm infants is 2.2–11mg/kg/day. Additional higher supplementation should be considered for infants with cholestasis.

Vitamin K (Phytonadione)

Vitamin K is a group of lipophilic, hydrophobic vitamins necessary for the synthesis of coagulation factors (factors II (prothrombin), VII, IX, and X, and the anticoagulation proteins C and S in the liver, as well as many other important functional proteins such as osteocalcin. Insufficient levels of vitamin K may lead to haematological complications, resulting in the impaired production of these active coagulation molecules (47, 48) and a subsequent increased risk of vitamin K deficiency bleeding (VKDB), which may be devastating.

Vitamin K deficiency is far more common in neonates compared to adults due to immaturity of the coagulation system, inadequate colonisation with Vitamin K-producing bacteria in the intestines, limited maternal transfer of vitamin K across the placenta, and low concentrations of the vitamin in breast milk (39). Exclusive human milk feeding is a risk factor for VKDB in otherwise-healthy preterm and term infants (40-42, 47-48), with a significant proportion of term infants showing evidence of subclinical Vitamin K deficiency at age 2-5 months related to breastfeeding duration (43-45, 46).

All preterm infants are offered prophylactic Vitamin K at birth, and those exclusively fed human milk receive sufficient extra Vitamin K from multi-nutrient milk fortifiers if given during the NICU stay, However, a preterm infant on full exclusive unfortified breastmilk feeds (150 mL/kg/day) receives only a minimal proportion of their currently recommended Vitamin K intake of 4.4-28 micrograms/kg/day (1). A recent prospective observational study in exclusively breastfed preterm infants who all received intramuscular prophylaxis at birth showed that some already had undetectable Vitamin K levels prior to discharge, and that the majority who remained exclusively breastfed post-discharge had developed biochemical evidence of functional subclinical Vitamin K deficiency by 2-3 months corrected age for both haematological and bone Vitamin K-dependent proteins (46).

Nutritional guidelines for preterm infants do not offer recommendations for Vitamin K supplementation after discharge, however more recent publications suggest a daily supplement of 50micrograms/day (not per kg) for all preterm infants born <37 weeks gestation being discharged exclusively on unfortified human milk feeds, for at least the first 3 months at home, in order to improve intakes in early infancy and guard against subsequent deficiency (23). Regional/local discussion should take place to inform policy.

Current multivitamin preparations used for preterm infants do not contain vitamin K, though there are a range of acceptable options for supplementation that can be implemented in line with unit preference and Integrated Care Board product availability (23). Options that would effectively deliver the equivalent of at least the minimum daily requirement of 50micrograms could include:

i) Konakion MM Paediatric® (phytomenadione 2mg /0.2 mL solution for injection; Neon Healthcare Ltd):, 2mg **given orally** once monthly.

ii) A single further Konakion MM Paediatric® 1mg intramuscular injection at discharge - this should last for up to 3 months and would avoid compliance issues but maybe far less acceptable to parents and babies (23).

iii) NeoKay oral drops® (Neoceuticals Ltd; 200microgram/mL VK_1): Give 50microgram (0.25mL via dropper) once daily to provide daily VK_1 intake comparable to that from formula milks which are supplemented to meet current recommendations (VK_1 content typically 60-80microgram/L); this product is a food supplement

Evidence to Support Iron Recommendations

Iron supplementation versus no supplementation

A systematic review of 8 trials, conducted in 7 countries and including 1093 infants (birth weight < 1.5kg and <32 weeks gestation), was conducted by the World Health Organization to examine the impact of iron supplementation on morbidity, growth, neurodevelopment and anaemia (3). Most trials involved comparing supplementation of 1-7mg/kg/day iron with a placebo or no iron supplementation (3). One trial compared a multivitamin and iron preparation with multivitamins alone (3). Iron supplementation was reported to have little or no effect on sepsis, necrotising enterocolitis, cognitive development or feed intolerance (very low certainty evidence) (3). It was associated with increased weight (very low certainty evidence) and length (moderate certainty evidence) (3). Iron supplementation was found to decrease prevalence of anaemia and increased haemoglobin (moderate certainty evidence) (3).

Low birth weight infants

There is evidence to show that babies with birth weights of 2-2.5kg (regardless of gestation) who are given iron supplements (1-2mg/kg/day) from 6 weeks to 6 months of age have a decreased risk of iron deficiency (36% vs 4%) and iron deficiency anaemia (10% vs 0%) at 6 months (55). In addition, the risk of iron deficiency at 12 months of age is also reduced (56). The follow up to this randomized controlled trial (RCT) showed that at 3½ years of age, those supplemented with iron had a significantly lower prevalence of behavioural problems than those in the placebo group (3% vs 13%) (56) and they had significantly lower scores in aggressive and rule-breaking (externalizing-type) behaviours and in thought problems at 7 years of age (57). It is recommended to give iron supplements to babies with birth weights of 2-2.5kg regardless of gestational age, at a dose of 1–2 mg/kg/day up to 6 months of age (2).

Starting iron supplementation

ESPGHAN updated their recommendation to start iron supplementation at 2 weeks of age, compared with their previous advice of starting at 2-4 weeks, following a meta-analysis conducted by Jin et al (58). This found starting iron supplementation at ~2-3 weeks vs later ~4-8 weeks of age is associated with less of a decrease in serum ferritin and haemoglobin levels and consequently a lower need for blood transfusions in preterm babies. Koletzko et al (2) also recommend initiation of iron at 2 weeks, following findings of improved haematological parameters with early initiation in babies born ≤1.3kg (59).

Discontinuing iron supplementation

ESPGHAN recommended that iron supplements are continued in preterm infants until 6–12 months of age (depending on diet) and that haemoglobin and serum ferritin should be monitored at follow-up visits (1).

Preterm and term infants should receive iron rich complementary foods (1,59). It is acknowledged iron fortified foods and iron supplements may be needed to meet requirements during the introduction of complementary foods (60). The source of dietary iron will impact on absorption with approximately 25% of animal or haem sources of iron absorbed (60). Non haem sources of iron are less well absorbed, and absorption is affected by other dietary factors which can facilitate or inhibit absorption (60).

Excess iron

ESPGHAN warns against prolonged intake of high doses of iron as there are no mechanisms for excretion of iron from the human body and therefore excess iron may have potential to have adverse effects. Such effects may cause oxidative injury in preterm babies which could exacerbate conditions such as necrotising enterocolitis and retinopathy of prematurity (2). This guideline advises against prolonged dietary iron intakes of >4mg/kg/day. However, some babies may require high doses of iron for short periods (e.g. babies on erythropoietin may require supplementation up to 6 mg/kg/day) (1).

Appendix 2: Available Multivitamin Preparations

Vitamin	Abidec® 0.3 mL*	Abidec® 0.6 mL*	DaliVit® 0.3 mL	DaliVit® 0.6 mL	Healthy Start 5 drops	Units
A	667 (200)	1333 (400)	2500 (750)	5000 (1500)	777 (233)	international units (microgram)
D	200 (5)	400 (10)	200 (5)	400 (10)	400 (10)	international units (microgram)
B1 (thiamine)	0.2	0.4	0.5	1	0	milligram
B2 (riboflavin)	400	800	200	400	0	micrograms
B3 (nicotinamide/niacin)	4	8	2.5	5	0	milligram
B6 (pyridoxine)	400	800	250	500	0	micrograms
C (ascorbic acid)	20	40	25	50	20	milligram

*Manufacturers guidance regarding Abidec® “Vitamin A palmitate contains refined peanut oil (Arachis oil) and should not be taken by patients known to be allergic to peanut. Patients with soya allergy should also avoid Abidec® Multivitamin Drops.”

Appendix 3: Alternative Vitamin Supplementation when shortage of first line products

Born <34weeks and/or <1.8kg	
Fortified breastmilk (Gold Prem® or Nutriprem® fortifier) (including fortified breastmilk feeding post discharge) **OR** Nutriprem® 1/ Gold Prem® 1	Colecalciferol (400IU/day)
Unfortified breastmilk (not recommended*)	DaliVit® 0.3mL/day **and** Colecalciferol (400IU/day) (consider Folic Acid 50microgram/day)
On reaching 1.8kg – 2kg or at discharge ** dependent upon local policy for change to nutrient enriched post discharge formulas	
Fortified breastmilk (Gold Prem® or Nutriprem® fortifier) (including fortified breastmilk feeding post discharge) **OR** Gold Prem® 2/ Nutriprem® 2 **OR** Term/Specialist/High Calorie Term Formula	Healthy Start (5 drops) **OR** Colecalciferol (400IU/day)
Unfortified breastmilk and/or breastfeeding	DaliVit® 0.6mL/day (consider vitamin K on discharge – see Appendix 1 for dosing)
Born 34-36^{+6} weeks and ≥1.8kg	
Breast milk	Healthy Start (5 drops) **OR** 400IU/day Colecalciferol (consider vitamin K on discharge – see Appendix 1 for dosing)
Term Formula	Healthy Start (5 drops) **OR** 400IU/day Colecalciferol

Appendix 4: Total vitamin A & D intakes by infant weight, milk choice and volume

	Nutriprem 1 & Abidec 0.3ml OD						Nutriprem 1 & Abidec 0.6ml OD							
	0.5kg		0.75kg		1kg		1.001kg		1.2kg		1.5kg		1.8kg	
mL/kg	**150**	**165**	**150**	**165**	**150**	**165**	**150**	**165**	**150**	**165**	**150**	**165**	**150**	**165**
Vitamin A (micrograms per kg per day)	947	1000	814	871	748	803	948	1003	881	936	815	870	770	825
Vitamin D (international units per kg per day)	586	605	452	470	386	404	585	604	520	537	452	470	408	426
	SMA Gold Prem 1 & Abidec 0.3ml OD						SMA Gold Prem 1 & Abidec 0.6ml OD							
	0.5kg		0.75kg		1kg		1.001kg		1.2kg		1.5kg		1.8kg	
mL/kg	**150**	**165**	**150**	**165**	**150**	**165**	**150**	**165**	**150**	**165**	**150**	**165**	**150**	**165**
Vitamin A (micrograms per kg per day)	893	942	760	809	694	743	894	943	827	877	761	811	716	767
Vitamin D (international units per kg per day)	604	624	470	490	404	424	604	624	537	557	470	490	426	446
	Fortified Breastmilk (Cow and Gate) & Abidec 0.3ml OD						Fortified Breastmilk (Cow and Gate) & Abidec 0.6ml OD							
	0.5kg		0.75kg		1kg		1.001kg		1.2kg		1.5kg		1.8kg	
mL/kg	**150**	**165**	**150**	**165**	**150**	**165**	**150**	**165**	**150**	**165**	**150**	**165**	**150**	**165**
Vitamin A (micrograms per kg per day)	833	877	700	744	634	678	834	878	767	811	701	745	656	700
Vitamin D (international units per kg per day)	730 (104%)	763 (109%)	596	629	530	563	730 (104%)	763 (109%)	663	696	596	629	552	585
	Fortified Breastmilk (SMA) & Abidec 0.3ml OD						Fortified Breastmilk (SMA) & Abidec 0.6ml OD							
	0.5kg		0.75kg		1kg		1.001kg		1.2kg		1.5kg		1.8kg	
mL/kg	**150**	**165**	**150**	**165**	**150**	**165**	**150**	**165**	**150**	**165**	**150**	**165**	**150**	**165**
Vitamin A (micrograms per kg per day)	1055 (106%)	1120 (112%)	922	987	856	921	1057 (106%)	1122 (112%)	989	1054 (105%)	923	988	879	943
Vitamin D (international units per kg per day)	643	667	509	533	443	467	643	667	576	600	509	533	465	489

Table 1: Total daily vitamin A (micrograms per kg per day) & vitamin D (international units per kg per day) intakes with dose banding by infant weight (Option 1) for infants ≤1.8kg

Please note: % are an expression of ESPGHAN requirements, where exceeded.

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	Nutriprem 1 & Abidec 0.6ml OD											
	0.5kg		0.75kg		1kg		1.2kg		1.5kg		1.8kg	
mL/kg	**150**	**165**	**150**	**165**	**150**	**165**	**150**	**165**	**150**	**165**	**150**	**165**
Vitamin A (micrograms per kg per day)	1349 (135%)	1404 (140%)	1082 (108%)	1137 (114%)	949	1004	881	936	815	870	770	825
Vitamin D (international units per kg per day)	986 (141%)	1004 (143%)	719 (103%)	737 (105%)	586	604	520	537	452	470	408	426
	SMA Gold Prem 1 & Abidec 0.6ml OD											
	0.5kg		0.75kg		1kg		1.2kg		1.5kg		1.8kg	
mL/kg	**150**	**165**	**150**	**165**	**150**	**165**	**150**	**165**	**150**	**165**	**150**	**165**
Vitamin A (micrograms per kg per day)	1295 (130%)	1344 (134%)	1028 (103%)	1077 (108%)	895	944	827	877	761	811	716	767
Vitamin D (international units per kg per day)	1004 (143%)	1024 (146%)	737 (105%)	757 (108%)	604	624	537	557	470	490	426	446
	Fortified Breastmilk (Cow and Gate) & Abidec 0.6ml OD											
	0.5kg		0.75kg		1kg		1.2kg		1.5kg		1.8kg	
mL/kg	**150**	**165**	**150**	**165**	**150**	**165**	**150**	**165**	**150**	**165**	**150**	**165**
Vitamin A (micrograms per kg per day) (ug/kg/d)	1235 (124%)	1279 (128%)	968	1012 (101%)	835	879	767	811	701	745	656	700
Vitamin D (international units per kg per day)	1130 (161%)	1163 (166%)	863 (123%)	896 (128%)	730 (104%)	763 (109%)	663	696	596	629	552	585
	Fortified Breastmilk (SMA) & Abidec 0.6ml OD											
	0.5kg		0.75kg		1kg		1.2kg		1.5kg		1.8kg	
mL/kg	**150**	**165**	**150**	**165**	**150**	**165**	**150**	**165**	**150**	**165**	**150**	**165**
Vitamin A (micrograms per kg per day)	1457 (146%)	1522 (152%)	1190 (119%)	1255 (126%)	1057 (106%)	1122 (112%)	989	1054 (105%)	923	988	879	943
Vitamin D (international units per kg per day)	1043 (149%)	1067 (152%)	776 (111%)	800 (114%)	643	667	576	600	509	533	465	489

Table 2: Total daily vitamin A (micrograms per kg per day) & vitamin D (international units per kg per day) intakes with a pragmatic approach (Option 2) for infants ≤1.8kg

Please note: % are an expression of ESPGHAN requirements, where exceeded.

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