NHS Grampian

NHS Grampian Staff Guideline For The Management Of Hypophosphataemia In Adults

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Policy Statement:

It is the responsibility of all staff to ensure that they are working to the most up to date and relevant guideline, policies, protocols and procedures.

Version 4

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Executive Sign-Off

This document has been endorsed by the Director of Pharmacy and Medicines Management

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Revision Date	Previous Revision Date	Summary of Changes (Descriptive summary of the changes made)	Changes Made (Identify page numbers and section heading)
April 2024	April 2022	Addition of introduction heading, classification titles amended, reference to section 5.2 added.	Introduction (P4)
April 2024	April 2022	Layout change, metabolic alkalosis, ferric carboxymaltose and salbutamol added, catecholamines changed to adrenaline/noradrenaline.	Causes of hypophosphataemia (P4)
April 2024	April 2022	Layout change, addition of irritability, somnolence, hallucinations and osteomalacia.	Signs and Symptoms of Hypophosphataemia (P5)
April 2024	April 2022	Addition of advice for considering oral replacement in mild, asymptomatic hypophosphataemia, titles amended.	Dosage and Administration (P6)
April 2024	April 2022	Addition of volume of water tablets to be dissolved in and sodium content and reference to local enteral guidance.	Phosphate-Sandoz® (P6)
April 2024	April 2022	Heading added, clarified setting for IV treatment, added licensing information.	Section 5.2 (P7)
April 2024	April 2022	Subtitle added, added advice for repeat infusions, advice for mild and moderate hypophosphataemia amended, ‘day’ changed to 24 hours.	Section 5.2.1 Phosphates Polyfusor® (P7)
April 2024	April 2022	Subtitle added, advice for mild and moderate hypophosphataemia amended.	Section 5.2.2 Sodium Glycerophosphate 21.6% (P8)
April 2024	April 2022	Further information provided regarding side effects via oral and IV routes. Categorisation of adverse effects, addition of tetany and convulsions, hypomagnesaemia, organ damage, cardiac arrhythmias. Removal oedema. Clarified metastatic calcification.	Adverse effects of phosphate replacement therapy (oral and IV) (P9)

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NHS Grampian Staff Guideline For The Management Of Hypophosphataemia In Adults

1. Introduction

This guideline is for use within primary or secondary care in NHS Grampian. Intravenous phosphate replacement should only be used in an acute setting, as outlined in section 5.2. Specialist areas may use an alternative replacement regimen (e.g. Gastroenterology) or alternative intravenous phosphate preparations (e.g. ICU, Haematology, Oncology). Alternative intravenous preparations are restricted to these areas due to their high potassium content.

The NHS Grampian reference range for serum phosphate in patients over 16 years of age is 0.8 - 1.5mmol/L. Serum phosphate level should be checked before commencing any treatment for hypophosphataemia.

Table 1. Serum phosphate classification

Normal (0.8 - 1.5mmol/L)	**Mild hypophosphataemia** (0.6 - 0.79mmol/L)	**Moderate hypophosphataemia** (0.3 - 0.59mmol/L)	**Severe hypophosphataemia** (<0.3mmol/L)

2. Causes of Hypophosphataemia [1-5]

Wherever possible, the cause of hypophosphataemia should be identified and corrected.

There are four major mechanisms by which hypophosphataemia can occur:

1) Redistribution of phosphate into cells

- Refeeding syndrome
- Severe diabetic ketoacidosis
- Metabolic or severe respiratory alkalosis
- Hepatic failure
- Septicaemia
- Medication, e.g. adrenaline/noradrenaline, insulin, salbutamol

2) Decreased intestinal absorption of phosphate

- Inadequate dietary intake
- Malnutrition due to malabsorption or persistent vomiting
- Vitamin D deficiency
- Chronic diarrhoea
- Medication, e.g. antacids (phosphate binder)

3) Increased renal phosphate excretion

- Alcoholism
- Medication, e.g. acetazolamide, theophylline, diuretics, ferric carboxymaltose
- Primary hyperparathyroidism
- Metabolic acidosis

4) Removal by renal replacement therapies

3. Signs and Symptoms of Hypophosphataemia [1-4,6]

Hypophosphataemia is often asymptomatic but clinical symptoms are more common when the serum phosphate level is below 0.3mmol/L.

Symptoms may include:

- Musculoskeletal: myopathy, muscle weakness, rhabdomyolysis (more likely in alcoholic patients)
- Cardiovascular: cardiomyopathy, arrhythmias
- Neurological: paraesthesia, irritability, somnolence, confusion, hallucinations, seizures*, encephalopathy, coma
- Haematological abnormalities
- Respiratory failure
- Osteomalacia (in chronic hypophosphataemia)

*Please note there is some evidence to suggest transient hypophosphataemia may occur as a result of a patient having a seizure, in particular generalised tonic-clonic seizures, which may not require replacement[12]. Please contact neurology for advice.

4. Precautions and Monitoring [3,6-10]

Phosphate should be used cautiously in patients with severe renal impairment (eGFR <30 ml/min/1.73m^2) as phosphate is renally excreted[8]. A dose reduction may be required – discuss with clinical pharmacist or renal specialists.

Some care is necessary with the interpretation of serum phosphate results as concentration falls transiently after high carbohydrate meals and substantial diurnal variation exists.

The rise in serum phosphate levels from any form of phosphate replacement therapy cannot be predicted. Therefore, monitoring is required.

Phosphate administration may lead to hypocalcaemia.

Consideration should be given to the potassium and sodium content of phosphate replacement therapies (listed under individual replacement therapies below).

Monitor electrolytes (i.e. phosphate, calcium, potassium, sodium and magnesium) frequently, e.g. 6-12 hourly during IV administration. Continue to monitor for several days after acute replacement.

5. Dosage and Administration [4,7-9,11,12]

Table 2. Treatment guidance

Severity of hypophosphataemia	Phosphate Level	Management required
Mild	0.6 – 0.79mmol/L and asymptomatic	Oral replacement can be considered*
Mild	0.6 – 0.79mmol/L and symptomatic	Intravenous replacement
Moderate	0.3 – 0.59mmol/L and asymptomatic	Oral replacement
Moderate	0.3 – 0.59mmol/L and symptomatic	Intravenous replacement
Severe	<0.3mmol/L	Intravenous replacement

*Decide if phosphate replacement is clinically necessary. Consider if the patient is at risk of further phosphate depletion.

5.1 Oral Phosphate Replacement Therapy

Phosphate Sandoz®[7]

Each tablet contains 16.1mmol phosphate, 20.4mmol sodium and 3.1mmol potassium.

These tablets are considered high in sodium. One tablet contains equivalent to 23% of the WHO recommended maximum daily intake of 2g sodium for an adult. The maximum daily dose of this product is equivalent to 141% of the WHO recommended maximum daily intake for sodium. This should be particularly taken into account for those on a low salt diet.

- 1-2 tablets up to 3 times a day (maximum 6 tablets per day).
- Tablets should be dissolved in 50-70mL of water.
- Monitor serum phosphate daily in secondary care. In primary care, monitor serum phosphate every 3-4 days or more frequently if clinically indicated.
- Adjust dose according to response.

Use of Phosphate Sandoz® to treat hypophosphataemia is off-label (except where hypophosphataemia is associated with vitamin D resistant rickets and vitamin D resistant hypophosphataemic osteomalacia), but no other UK licensed oral preparations are available.

For patients with enteral feeding tubes who require enteral phosphate replacement, please refer to the Guidelines For The Administration Of Medicines To Adults Via Enteral Tubes Within NHS Grampian.

Note:

- Do not give at the same time as antacids, as this may reduce absorption of phosphate and therefore reduce efficacy.
- Diarrhoea is a common side-effect – give with plenty of water to minimise risk. Reduce the dose if this occurs.

5.2 Intravenous Phosphate Replacement Therapy

Intravenous phosphate replacement should only be used in an acute setting.

Treatment Options

Phosphates Polyfusor® is licensed for the treatment of moderate to severe hypophosphataemia and should be used first line when IV administration is indicated.

Sodium glycerophosphate 21.6% can be used as an alternative to Phosphates Polyfusor® if there are supply issues with the Polyfusor®. The licensed indication for sodium glycerophosphate is as a supplement to parenteral nutrition.

5.2.1 Phosphates Polyfusor® [1,12,13]

500mL Polyfusor® contains 50mmol phosphate, 81mmol sodium and 9.5mmol potassium.

Doses below are for patients with normal renal function.
(Table adapted from Taylor *et al* and Polyfusor® SPC) [1,14]

Administer appropriate dose over 6 - 12 hours.

Table 3. Suggested doses of Phosphates Polyfusor®

Serum phosphate concentration (mmol/L)	**Weight 40 - 60kg**		**Weight 61 - 80kg**		**Weight 81kg and over**	
	Amount of phosphate	**Volume of Polyfusor®**	**Amount of phosphate**	**Volume of Polyfusor®**	**Amount of phosphate**	**Volume of Polyfusor®**
<0.3 Severe	30mmol	300mL	40mmol	400mL	50mmol	500mL
0.3 – 0.59 Moderate (if symptomatic or oral/enteral route is unavailable and treatment is essential)	20mmol	200mL	30mmol	300mL	40mmol	400mL
0.6 - 0.79 Mild (if symptomatic or oral/enteral route is unavailable and treatment is essential)	10mmol	100mL	15mmol	150mL	20mmol	200mL

Additional Prescribing Notes:

- Take care to ensure that only the prescribed volume is delivered from the Polyfusor®. Discard the remainder.
- Max flow rate: 15mmol per hour (150mL per hour).
- Maximum of 50mmol (500mL) per 24 hours.
- Patients with severe hypophosphataemia may require repeat infusions over subsequent days.
- Use a dedicated IV lumen for Polyfusor® as it may cause precipitation if administered with other drugs. It may be administered peripherally.

Monitor during IV administration:

- Electrolytes (i.e. phosphate, calcium, potassium, sodium and magnesium) frequently, e.g. 6-12 hourly
- Renal function
- Blood pressure
- Fluid balance
- ECG
- Acid-base balance

5.2.2 Sodium Glycerophosphate 21.6% concentrate for solution for infusion [13,15]

Sodium Glycerophosphate 21.6% concentrate for solution for infusion should not be given to patients in a state of dehydration or with hypernatraemia, hyperphosphataemia, severe renal insufficiency or shock.

Each 20mL vial contains 20mmol phosphate and 40mmol sodium and **must be diluted prior to use with sodium chloride 0.9% or glucose 5%.**

Doses below are for patients with normal renal function.

Administer appropriate dose over at least 8 hours.

Table 4. Suggested doses of sodium glycerophosphate 21.6%

For Peripheral Administration (Max concentration 0.1mmol/mL Phosphate)						
Serum phosphate concentration (mmol/L)	**Weight 40 - 60kg**		**Weight 61 - 80kg**		**Weight 81 - 120kg**	
	Volume of sodium glycero-phosphate 21.6% concentrate for infusion	Suggested dilution volume	**Volume of sodium glycero-phosphate 21.6% concentrate for infusion**	Suggested dilution volume	**Volume of sodium glycero-phosphate 21.6% concentrate for infusion**	Suggested dilution volume
<0.3 Severe	30mL= 30mmol	500mL (0.06mmol/mL)	40mL= 40mmol	500mL (0.08mmol /mL)	50mL= 50mmol	500mL (0.1mmol/mL)
0.3 – 0.59 Moderate (if symptomatic or oral/enteral route is unavailable and treatment is essential)	20mL= 20mmol	250mL (0.08mmol/mL)	30mL= 30mmol	500mL (0.06mmol /mL)	40mL= 40mmol	500mL (0.08mmol/mL)
0.6 - 0.79 Mild (if symptomatic or oral/enteral route is unavailable and treatment is essential)	10mL= 10mmol	100mL (0.1mmol/mL)	15mL= 15mmol	250mL (0.06mmol /mL)	20mL= 20mmol	250mL (0.08mmol/mL)

Additional Prescribing Notes:

- If a more concentrated solution is to be given (i.e. 0.2-0.4mmol/mL) then this must be given centrally due to high osmolality
- Monitoring as for Phosphates Polyfusor®

6. Adverse effects of phosphate replacement therapy (oral and IV) [1,3,6,8]

Apart from gastro-intestinal upsets, nausea and diarrhoea (may require dose reduction), very few side effects have been reported with oral replacement therapy. These side effects are also associated with intravenous replacement therapy.

The following side effects are more prevalent with intravenous administration but could theoretically occur by any route of administration:

- Electrolyte disturbance
  - Hyperphosphataemia (particularly in patients with renal failure)
  - Hypocalcaemia (may be severe, with tetany and convulsions)
  - Hyperkalaemia (due to potassium content of replacement therapy)
  - Hypernatraemia
  - Hypomagnesaemia
- Metastatic calcification (particularly with initial hypercalcaemia)
  - May cause hypotension and organ damage
  - Can result in acute renal failure

- Cardiac arrhythmias
- Dehydration

With intravenous administration:
- Phlebitis

If any of these adverse effects occur, contact the prescriber for review, as further monitoring may be required and treatment may need to be adjusted or withheld.

7. References

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8. Responsibilities for implementation

Organisational:	Chief Executive and Management Teams
Corporate:	Senior Managers
Departmental:	Heads of Service/Clinical Leads
Area:	Line Managers
Hospital/Interface services:	Group Clinical Directors
Operational Management Unit:	Unit Operational Managers