

## NOTTINGHAMSHIRE AREA PRESCRIBING COMMITTEE SHARED CARE PROTOCOL AGREEMENT

### Phosphate Binders for the Treatment of Hyperphosphataemia in adults with Chronic Kidney Disease

#### OBJECTIVES

To outline referral criteria for shared care, define the responsibilities of the specialist and the GP, and provide prescribing information.

#### REFERRAL CRITERIA

- Prescribing responsibility will only be transferred when it is agreed by the specialist and the patient's primary care prescriber, that **the patient's condition is stable**.

#### PROCESS FOR TRANSFERRING PRESCRIBING TO PRIMARY CARE

- Requests for shared care should include individual patient information (that outlines all relevant aspects of the patient's care) and directions to the appropriate information sheets at [www.nottsapc.nhs.uk](http://www.nottsapc.nhs.uk).
- If the GP does not agree to shared care, then he/she will inform the specialist of his/her decision in writing within 14 days.
- In cases where problems arise with the shared care agreement and patient care is affected, the responsibility for the patient's management (including prescribing) will revert back to the specialist.

#### BACKGROUND INFORMATION

A number of oral phosphate binders are available which may be used in the context of a multiple therapeutic approach, these include calcium containing binders (calcium acetate (Phosex<sup>®</sup> and Renacet<sup>®</sup>) and calcium carbonate (Calcichew<sup>®</sup>)) and non-calcium containing binders (sevelamer carbonate (generic), lanthanum carbonate (Fosrenol<sup>®</sup>), sucroferric oxyhydroxide (Velphoro<sup>®</sup>) and aluminium hydroxide (Alu-Cap Capsules<sup>®</sup>). These products may be used in combination with vitamin D analogues (alfacalcidol or calcitriol) and/or cinacalcet (Mimpara<sup>®</sup>), to control the development of hyperparathyroidism and renal bone disease.

Calcium-based phosphate binders are generally used as initial therapy for patients with chronic kidney disease because they are cheap and relatively efficacious; they should always be used in conjunction with dietary phosphate restriction to control phosphate levels.

Where possible, calcium acetate (Phosex<sup>®</sup> or Renacet<sup>®</sup>) should be used as the first line phosphate binder. Calcium carbonate (Calcichew<sup>®</sup>) should be used in patients who require a chewable tablet. Non-calcium containing phosphate binders are generally used if hypercalcaemia develops with the use of calcium-containing phosphate binders, calcium-containing phosphate binders are not tolerated, or where patients are at high risk of/or have evidence of established vascular calcification or low turnover bone disease. Generic sevelamer carbonate should be used as the most cost effective second line non-calcium containing phosphate binder. Lanthanum

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carbonate and sucroferric oxyhydroxide are available as third line agents. Aluminium based phosphate binders are rarely used and if they are, then aluminium levels must always be checked due to the risk of aluminium accumulation.

### NATIONAL/ LOCAL GUIDANCE

Chronic kidney disease early identification and management of chronic kidney disease in adults in primary and secondary care Issued: July 2014 **NICE** clinical guideline **182**

Available from <https://www.nice.org.uk/guidance/cg182>

NICE Clinical Guideline 157 – Chronic Kidney Disease (Stage 4 or 5): management of hyperphosphataemia. March 2013. Available from <https://www.nice.org.uk/Guidance/CG157>

Detailed guidelines exist within NUH for the management of bone and mineral metabolism in patients with CKD; this includes guidance on the use of phosphate binders, vitamin D analogues and calcimimetics.

### CLINICAL INFORMATION

See Phosphate Binders Prescribing Information Sheet

### AREAS OF RESPONSIBILITY

#### Specialist's Roles and Responsibilities

1. The specialist will confirm the diagnosis of hyperphosphataemia and arrange initial renal dietetic assessment.
2. The specialist will recommend and initiate treatment and discuss the benefits and side effects of treatment with the patient.
3. The specialist will counsel the patient on the importance of compliance with medication and dietetic advice.
4. The specialist will ensure that the patient has an adequate supply of medication (28 days) until shared care arrangements are in place. Further prescriptions will be issued by the specialist if for any unforeseen reason, arrangements for shared care are not in place at the end of 28 days.
5. If shared care is considered appropriate for the patient, and the patient's treatment and condition are stable, the specialist will contact the GP.
6. The specialist will provide the patient's GP with the following information:
  - diagnosis of the patient's condition with the relevant clinical details
  - details of the patient's treatment to date
  - details of treatments to be undertaken by the GP\*
  - details of other treatments that the patient is receiving that are not included in the shared care agreement
  - details of monitoring arrangements
7. In general, patients prescribed oral phosphate binders will have advanced chronic kidney disease or be on dialysis, and as such will remain under long term secondary care follow up.

\*Including reasons for choice of treatment, drug and/or combination of drugs, frequency of treatment, and number of months of treatment to be given before review by the consultant.

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Pragmatically the majority of monitoring is likely to take place in secondary care and the renal team will communicate any dose changes or amendments to the patient's GP.

8. Whenever a patient is reviewed, the specialist will:
  - send a written summary to the patient's GP within 14 days
  - communicate any dose changes or drug changes to the patient
9. The specialist team will provide training for primary care prescribers if necessary, to support the use of the shared care agreement.
10. Contact details for designated members of the NUH renal team will be available for primary care prescribers.
11. Details for fast track referral back to secondary care will be supplied.
12. The specialist will provide the patient with details of their treatment; follow up appointments, monitoring requirements and nurse specialist contact details.

### **Primary Care Prescriber's Roles and Responsibilities**

1. Ensure that he/she has the information and knowledge to understand the therapeutic issues relating to the patient's clinical condition.
2. Undertake any additional training necessary in order to carry out a practice based service.
3. Agree that in his/her opinion the patient should receive shared care for the diagnosed condition, unless good reasons exist for the management to remain with secondary care.
4. If the GP does not agree with shared care, he/she will inform the specialist of his/her decision in writing within 14 days.
5. Prescribe maintenance therapy in accordance with the written instructions from the specialist, and communicate any changes of dose made in primary care to the patient. It is the responsibility of the prescriber that makes any dose change to communicate this to the patient.
6. Patients receiving oral phosphate binders will generally remain under secondary care follow-up. Clinical monitoring will normally be undertaken in secondary care and secondary care clinicians will advise the patient and primary care practitioner of any required changes to therapy. Primary care clinicians are responsible for taking action on results requested in primary care, with advice from renal unit clinicians if necessary.
7. Report any adverse effect(s) to treatment to the secondary care specialist.
8. The GP will ensure that the patient is monitored in accordance with the prescribing information included with this shared care agreement, and will take the advice from the specialist if there are any amendments to the suggested monitoring schedule.
9. The GP will ensure that the patient is given the appropriate appointments for follow up and monitoring, and that defaulters from follow up are contacted to arrange alternative appointments. The GP should ensure that the patient understands the need to attend follow up appointments. It is the GPs responsibility to decide whether to continue treatment in a patient who does not attend appointments required for follow up and monitoring.

## REFERENCES

Detailed guidelines exist within NUH for the management of bone and mineral metabolism in patients with CKD; this includes guidance on the use of phosphate binders, vitamin D analogues and calcimimetics. These guidelines are available on the joint formulary website.

## ORIGINAL AUTHORS 2010

- Dr Simon Roe, Consultant Nephrologist, Nottingham University Hospitals NHS Trust.
- Judith Gregory, Renal Pharmacist, Nottingham University Hospitals NHS Trust.
- Nicky Bird, Pharmacist Manager, NHS Nottinghamshire County.

## IN CONSULTATION WITH

Consultant Nephrologists, Nottingham University Hospitals NHS Trust

The original version of this shared care protocol was produced using the Derbyshire Joint Area Prescribing Committee Shared Care Agreement for Phosphate Binders in the Treatment of Hyperphosphataemia in Patients on Dialysis.

## Updated August 2017

The following updates have been made to this shared care protocol:

- Addition of Renacet<sup>®</sup> 950mg tablets, for use in patients that are unable to obtain supplies of Phosex<sup>®</sup> 1g tablets from their community pharmacist.
- Addition of sucroferric oxyhydroxide (Velphoro<sup>®</sup>) as a third line phosphate binder.

## CONTACT DETAILS

	Base	Contact Details
Dr Simon Roe, Consultant Nephrologist	NCH Campus, Nottingham University Hospitals NHS Trust	0115 9691169 ext. 54438
Bruno Mafriaci, Specialist Renal Dietitian	NCH Campus, Nottingham University Hospitals NHS Trust	0115 9691169 ext. 57139 or Bleep 780-7076
Ian Hogg, Specialist Clinical Pharmacist – Renal (Adults)	NCH Campus, Nottingham University Hospitals NHS Trust	0115 9691169 Bleep 780-7078

## Phosphate Binders

### Traffic light classification- Amber 1 Information Sheet for Primary Care Prescribers

#### Licensed Indications

Calcium Carbonate (Calcichew<sup>®</sup>), Calcium Acetate (Phosex<sup>®</sup>), Calcium Acetate (Renacet<sup>®</sup>), Aluminium Hydroxide (Alu Cap Capsules<sup>®</sup>), Sevelamer Carbonate (generic), Lanthanum Carbonate (Fosrenol<sup>®</sup>) and Sucroferric Oxyhydroxide (Velphoro<sup>®</sup>) are all licensed as phosphate binders in adults with chronic kidney disease, in patients receiving dialysis. Sevelamer Carbonate (generic), Lanthanum Carbonate (Fosrenol<sup>®</sup>) and Aluminium Hydroxide (Alu Cap Capsules<sup>®</sup>), are also licensed as phosphate binders in adult patients with chronic kidney disease that are not on dialysis.

#### Prescribing outside of licensed Indications

Calcium Carbonate (Calcichew<sup>®</sup>), Calcium Acetate (Phosex<sup>®</sup>) and Calcium Acetate (Renacet<sup>®</sup>) are not licensed in pre-dialysis patients with chronic kidney disease; there is however, substantial experience of clinical use in this population. There is limited clinical experience of using Sucroferric Oxyhydroxide (Velphoro<sup>®</sup>) in pre-dialysis patients with chronic kidney disease.

#### Inclusion Criteria

This shared care agreement covers adult patients with chronic kidney disease under the care of the Nottingham Renal Unit.

#### Therapeutic Summary

Phosphate Binders are indicated for the control of hyperphosphataemia in adult patients with chronic kidney disease.

#### Medicines Initiation

Oral phosphate binders will be initiated by Consultants or Speciality Registrars in adult renal medicine, usually with input from a specialist renal dietitian.

#### Products Available

Calcium Carbonate (Calcichew<sup>®</sup>), Calcium Acetate (Phosex<sup>®</sup>), Calcium Acetate (Renacet<sup>®</sup>), Aluminium Hydroxide (Alu Cap Capsules<sup>®</sup>), Sevelamer Carbonate (generic), Lanthanum Carbonate (Fosrenol<sup>®</sup>) and Sucroferric Oxyhydroxide (Velphoro<sup>®</sup>).

#### Dosages and Route of Administration

See specific prescribing information included in pages 7 to 10.

#### Duration of Treatment

Treatment will be continued indefinitely.

#### Monitoring Requirements and Responsibilities

The SPC's for oral phosphate binders recommend monitoring levels of serum phosphorus and calcium. Patients that receive phosphate binders will have their phosphorus, calcium and parathyroid hormone levels measured at least every 3 months in secondary care.

**Explicit Criteria for Review and Discontinuation of Medicines**

Target biochemical parameters are described in the table below.

Biochemical Parameter	CKD Stage		
	3-4 GFR 15-59	5 non dialysis GFR <15	5 dialysis GFR <15
<b>Calcium</b>	Within normal range 2.2-2.6 mmol/l	Within normal range 2.2-2.6 mmol/l	Within normal range (Ideally 2.2-2.5 mmol/l)
<b>Phosphate</b>	0.9–1.5 mmol/l Aim towards normal range	0.9–1.5 mmol/l Aim towards normal range	1.1–1.7 mmol/l Aim towards normal range
<b>PTH</b>	Optimal levels not known	Optimal levels not known	144-648 ng/l <sup>1</sup>

Suggested actions based on abnormal biochemistry results

Abnormal Result	Suggested action
Phosphate > 1.7	Review concordance with prescribed binders Discuss dose increase / dietetic review with specialist
Phosphate < 1.1	Discuss dose reduction with specialist
Calcium > 2.6	Discontinue alfacalcidol or calcitriol Discontinue calcium containing phosphate binders Discuss with specialist
Calcium > 2.55	Discuss with specialist Reduce dose or discontinue alfacalcidol or calcitriol Consider dose reduction or discontinuation of calcium containing phosphate binders Consider introduction of non-calcium containing phosphate binder

**Contraindications**

See specific prescribing information included in pages 7 to 10.

**Precautions**

Calcichew – phenylketonuria, fructose intolerance, glucose-galactose malabsorption, sucrase-isomaltase insufficiency, history of renal calculi

Sevelamer – active inflammatory bowel disease, major GI surgery, GI motility disorders

Lanthanum – Acute peptic ulcer, inflammatory bowel disease, bowel obstruction, reduction in bile flow, paediatrics. Abdominal x-rays of patients taking lanthanum carbonate may have a radio-opaque appearance typical of an imaging agent.

All – pregnancy and lactation

**Clinically Relevant Drug Interactions and Suggested Management**

See specific prescribing information included in pages 7 to 10.

**Information Provided to Patients**

Patients are given verbal and written advice on dietary restriction of phosphate and are also counselled how to take phosphate binders.

Phosphate binder	Dose	Comments	Adverse effects	Contraindications	Clinically significant drug interactions
<b>Calcium Carbonate (Calcichew<sup>®</sup>)</b>	<p>Chewable tablets containing 1.25g calcium carbonate (equivalent to 500mg elemental calcium).</p> <p>Dose: one tablet with meals up to a maximum recommended dose of 3 x 1.25g tablets per day (due to higher elemental calcium content).</p>	<p>The tablets should be taken just before or during each meal (<b>NB not after meals</b>). Tablets may be chewed or sucked.</p>	<p>Hypercalcaemia and hypercalcuria. Constipation, flatulence, nausea, abdominal pain and diarrhoea.</p>	<p>Calcium salts are contraindicated in hypercalcaemia and hypercalciuria. Nephrolithiasis.</p>	<p>The Summary of Product Characteristics (SPCs) for calcium-based phosphate binders recommend that serum calcium should be regularly monitored during concomitant use of thiazide diuretics, as these reduce the urinary excretion of calcium. Systemic corticosteroids reduce calcium absorption so it may be necessary to increase the dose of calcium carbonate. Calcium-based phosphate binders reduce the absorption of concomitantly administered tetracycline, quinolones, and bisphosphonates.</p>
<b>Calcium Acetate (Phosex<sup>®</sup>),</b>	<p>Tablets containing 1g of calcium acetate (equivalent to 250mg elemental calcium).</p> <p>An initial starting dose of three tablets per day, distributed according to phosphate content of meals. The dose can be increased until the desired serum phosphate level is achieved, as long as hypercalcaemia does not occur.</p> <p>Most patients require 4 to 6 tablets per day (1 to 2 tablets with each meal).</p>	<p>The tablets should be swallowed whole with a meal to achieve the maximal phosphate binding effect; <b>do not chew</b>.</p> <p><b>Phosex<sup>®</sup> is recommended as the first line phosphate binder; it is more effective than Calcichew<sup>®</sup> and contains less elemental calcium.</b></p> <p>Renacet<sup>®</sup> 475mg is a smaller tablet than Phosex<sup>®</sup> 1g tablets and some patients find this easier to swallow.</p>	<p>Hypercalcaemia and hypercalcuria. Constipation, flatulence, nausea, abdominal pain and diarrhoea.</p>	<p>Calcium salts are contraindicated in hypercalcaemia and hypercalciuria</p>	<p>The Summary of Product Characteristics (SPCs) for calcium-based phosphate binders recommend that serum calcium should be regularly monitored during concomitant use of thiazide diuretics, as these reduce the urinary excretion of calcium. Systemic corticosteroids reduce calcium absorption so it may be necessary to increase the dose of calcium carbonate. Calcium-based phosphate binders reduce the absorption of concomitantly administered tetracycline, quinolones, and bisphosphonates.</p>

<p><b>Calcium Acetate (Renacet®)</b></p>	<p>Renacet 475mg Tablets containing 475mg of calcium acetate (equivalent to 120.25mg of elemental calcium) and Renacet 950mg Tablets containing 950mg of calcium acetate (equivalent to 240.5mg of elemental calcium).</p> <p>The Initial dose should be 475mg to 950mg with meals adjusted according to dietary intake.</p> <p>Titrate dose with meals and snacks according to serum phosphate levels.</p> <p>Maximum recommended dose of 14 x 475mg or 7 x 950mg tablets per day.</p>	<p>The elemental calcium content of Renacet® 475mg Tablets is 50% less than Phosex® 1g Tablets therefore the number of tablets required to be taken with each meal may be greater.</p> <p>Renacet® 950mg Tablets were added to the formulary in 2017 as an alternative to Phosex 1g Tablets for patients that are unable to obtain supplies of Phosex® from their community pharmacist.</p>			
<p><b>Aluminium Hydroxide (Alu Cap Capsules®)</b></p>	<p>Capsules containing 475 mg dried aluminium hydroxide.</p> <p>Dose may range from 4 to 20 capsules daily (approximately 2 to 10g dried aluminium hydroxide gel).</p>	<p>The capsules should be taken before meals.</p> <p><b>Generally reserved for short term use in patients with severe and difficult to control hyperphosphataemia.</b></p> <p><b>Ideally, the maximum duration of treatment should not exceed 6 months.</b></p>	<p>Aluminium hydroxide use in patients with chronic kidney disease may cause hyperalumaemia. Aluminium accumulates in the bone, lungs and nerve tissue. Aluminium accumulation in the CNS may be the cause of dialysis dementia which sometimes occurs in chronic kidney disease patients, receiving long term aluminium therapy for hyperphosphataemia. Constipation.</p>	<p>Aluminium salts are contra-indicated in hyperalumaemia and acute porphyria</p>	<p>The Summary of Product Characteristics (SPC) recommends that aluminium hydroxide reduces absorption of tetracyclines, quinolones, and vitamins, and may delay the absorption of quinidine.</p>



Phosphate binder	Dose	Comments	Adverse effects	Contraindications	Clinically significant drug interactions
<b>Sevelamer Carbonate (generic)</b>	<p>800mg film coated tablets.</p> <p>Initial dose should be 2400 to 4800mg daily, in 2 to 3 divided doses.</p> <p>The dose should be adjusted according to serum phosphate concentration.</p>	<p>Patients should take sevelamer with meals.</p> <p><b>Most cost effective second line phosphate binder; used for patients intolerant of calcium containing phosphate binders, those with baseline hypercalcaemia, and those who develop hypercalcaemia and/or suppressed PTH levels, on calcium containing binder therapy.</b></p>	<p>Nausea and vomiting, diarrhoea, dyspepsia, flatulence, upper abdominal pain, and constipation.</p>	<p>Sevelamer is contra-indicated in patients with bowel obstruction</p>	<p>The SPC recommends that sevelamer should not be taken simultaneously with ciprofloxacin. As sevelamer may affect the absorption of other medicinal products, where a reduction in bioavailability may have a clinically significant effect, the physician should consider monitoring blood levels.</p>
<b>Lanthanum Carbonate (Fosrenol®)</b>	<p>Chewable tablets containing 500mg, 750mg or 1000mg Lanthanum Carbonate.</p> <p>Sachets containing 750mg or 1000mg lanthanum carbonate oral powder.</p> <p>Control of serum phosphate level has been demonstrated at doses starting from 750 mg per day. The maximum dose studied in clinical trials, in a limited number of patients, is 3750 mg.</p>	<p>Lanthanum should be taken with or immediately after food, with the daily dose divided between phosphate containing meals.</p> <p>Tablets must be chewed and not swallowed whole. The contents of sachets should be sprinkled on soft food; lanthanum oral powder is insoluble and must not be mixed with liquid.</p> <p>Serum phosphate levels should be monitored and the dose of lanthanum titrated every two to three weeks until an acceptable serum phosphate level is reached,</p>	<p>Clotting of the haemodialysis graft, myalgia and cough.</p>	<p>Lanthanum is contra-indicated in pregnancy.</p>	<p>The SPC for lanthanum recommends that compounds known to interact with antacids should not be taken within two hours of lanthanum. Interactions with tetracyclines and quinolones are theoretically possible.</p>

<b>Lanthanum Carbonate (Fosrenol®) continued</b>	Patients who respond to lanthanum therapy usually achieve acceptable serum phosphate levels at doses of 1500mg to 3000mg lanthanum per day.	with regular monitoring thereafter.  <b>Third line phosphate binder therapy; may be used as a therapeutic switch in patients unable to tolerate sevelamer carbonate or those requiring high doses of sevelamer carbonate to improve concordance and reduce pill burden.</b>			
<b>Sucroferric oxyhydroxide (Velphoro®)</b>	Chewable tablets containing 500mg sucroferric oxyhydroxide.  Starting dose is 500mg with each meal.  Maximum daily dose is 3000mg (6 tablets).	Sucroferric oxyhydroxide should be taken with food, with the daily dose divided between phosphate-containing meals.  Tablets must be chewed and not swallowed whole.  <b>Third line phosphate binder therapy; may be used as a therapeutic switch for dialysis patients unable to tolerate sevelamer carbonate or those requiring high doses of sevelamer carbonate to improve concordance and reduce pill burden.</b>	Diarrhoea and discoloured faeces.	Haemochromatosis and any other iron accumulation disorders.	The SPC recommends that when administering any medicinal product that is already known to interact with oral iron therapy (e.g. alendronate, tetracyclines and quinolones) or has the potential to interact (e.g. levothyroxine), these drugs should be administered at least one hour before, or two hours after Velphoro®.