Phosphate Binders

Traffic light classification- Amber 1
Information sheet for Primary Care Prescribers

Licensed Indications
Calcium carbonate (Calcichew®), calcium acetate (Phosex®), calcium acetate (Renacet®), sevelamer carbonate (generic), lanthanum carbonate (generic) and sucroferric oxyhydroxide (Velphoro®) are all licensed as phosphate binding agents for the correction of hyperphosphataemia associated with CKD in patients undergoing dialysis. Sevelamer and lanthanum carbonate are also licensed in patients with CKD, not on dialysis, in whom a low phosphate diet alone is insufficient to control serum phosphate levels.

Prescribing outside of licensed indication
Calcium carbonate (Calcichew®), calcium acetate (Phosex®), calcium acetate (Renacet®) and sucroferric oxyhydroxide (Velphoro®) are not licensed for use in patients with CKD who are not undergoing dialysis; however, there is a substantial experience of clinical use in this population.

Any exclusions
This shared care agreement covers adult patients with CKD under the care of the Nottingham Renal Unit.

Therapeutic Summary
Phosphate Binders are indicated for the control of hyperphosphataemia in adult patients with CKD.

Medicines Initiation
Oral phosphate binders will be initiated by Consultants or Speciality Registrars in renal medicine, usually with input from Specialist Renal Dietitians.

Products available
Calcium carbonate (Calcichew®), calcium acetate (Phosex®), calcium acetate (Renacet®), sevelamer carbonate (generic), lanthanum carbonate (generic) and sucroferric oxyhydroxide (Velphoro®).

Dosages and route of administration
See table I.

Duration of treatment
Treatment may be continued indefinitely.

Monitoring Requirements and Responsibilities
The SPC recommends monitoring levels of serum phosphorus and calcium.
Patients receiving phosphate binders will have their phosphorus, calcium and parathyroid hormone levels measured at least quarterly in the hospital environment.

Criteria for Review and Discontinuation of Medication

Target biochemical parameters are described in the table below.

	CKD Stage		
Biochemical Parameter	**3-4 GFR 15-59**	**5 non-dialysis GFR <15**	**5D dialysis**
Calcium	Maintain close to normal range and avoid hypercalcaemia.	Maintain close to normal range and avoid hypercalcaemia.	Maintain close to normal range and avoid hypercalcaemia.
Phosphate	Suggest towards normal range.	Suggest towards normal range.	Suggest towards normal range.
PTH	Optimal range unknown. Aim for normal range (14-72 ng/l)	Optimal range unknown. Allow PTH levels to rise towards range in stage 5D (144 - 648 ng/l)	Optimal range unknown. Suggest 144 - 648 ng/l

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 the Specialist
Calcium > 2.6	Discontinue alfacalcidol or calcitriol Discontinue calcium-containing phosphate binders Discuss with Specialist
Calcium >2.55	Discuss with Specialist Reduce the dose or discontinue alfacalcidol or calcitriol Consider dose reduction or discontinuation of calcium-containing phosphate binders Consider the introduction of non-calcium-containing phosphate binder

Contraindications See table I.

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 medicine interactions and their management
See table I.

Information given to patient
Patients are given both verbal and written advice on dietary restriction of phosphate. Patients are counselled on how to take phosphate binders in relation to their meals.

Table I. Phosphate binder

Phosphate binder	Dose	Comments	Adverse effects	Contraindications	Clinically significant drug interactions	Monitoring requirements
Calcium Carbonate (Calcichew®)	Chewable tablets containing 1.25g calcium carbonate (500mg elemental calcium) per tablet. Dose as required by the individual patient depending on serum phosphate level. Generally, avoid doses > 1 tablet TDS due to high elemental calcium intake.	The tablets should be taken just before or during each meal. (NB, not after meals). Tablets may be chewed or sucked	Hypercalcaemia and hypercalciuria. Constipation, flatulence, nausea, abdominal pain and diarrhoea.	Calcium salts are contra-indicated in hypercalcaemia and hypercalciuria nephrolithiasis	The SPC for calcium-based phosphate binders recommends 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 may interfere with the absorption of concomitantly administered tetracycline preparations, quinolones and bisphosphonates.	The SPC recommends monitoring levels of serum phosphorus and calcium. Patients receiving phosphate binders will have their phosphorus, calcium and parathyroid hormone levels measured at least quarterly in the hospital environment.
Calcium Acetate (Phosex®)	Tablets containing 1000mg calcium acetate (250mg of elemental calcium) per tablet. An initial starting dose of three tablets daily distributed according to the phosphate content of meals. The dose can be increased until the desired serum phosphate level is achieved, as long as hypercalcaemia does not occur. Most patients require 4 to 6 tablets per day (1 to 2 tablets with each meal).	The tablets should be swallowed whole with a meal to achieve the maximal phosphate binding effect. Do not chew. **Phosex® is recommended as one of the first-line phosphate binders at NUH; it is more effective than Calcichew® and contains less elemental calcium.** Renacet® 475mg tablets are smaller tablets, and some patients find these easier to swallow than larger Phosex® or Renacet® 950mg tablets. The elemental calcium content of Renacet® 475mg tablets is less than Phosex®. Therefore, the number of tablets required with each meal may be greater. Renacet® 950mg tablets can be considered interchangeable with Phosex® 1g tablets if there are supply problems with either preparation.	Hypercalcaemia and hypercalciuria. Constipation, flatulence, nausea, abdominal pain and diarrhoea.	Calcium salts are contra-indicated in hypercalcaemia and hypercalciuria		
Calcium Acetate (Renacet®)	Tablets containing calcium acetate 475mg and 950mg (120.25mg to 240.5mg elemental calcium) per tablet. Starting dose is normally 1 tablet three times a day for patients with CKD and 2 tablets three times a day for dialysis patients. Most patients need 1 to 2 950mg tablets or 2 to 4 475mg tablets with each meal.					

Phosphate binder	Dose	Comments	Adverse effects	Contraindications	Clinically significant drug interactions	Monitoring requirements
Sevelamer Carbonate (generic)	800mg tablet. For patients who are not already on phosphate binders, the dosage is determined individually based on serum phosphate concentrations (refer to the SPC for further details).	Patients should take sevelamer with meals and adhere to dietary advice. **Can be used as a first-line phosphate binder; used for patients intolerant of calcium-containing phosphate binders or those with baseline hypercalcaemia or who develop hypercalcaemia and/or suppressed PTH levels on calcium-containing binder therapy.**	Nausea and vomiting, diarrhoea, dyspepsia, flatulence, upper abdominal pain, constipation.	Sevelamer is contra-indicated in patients with bowel obstruction.	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.	The SPC recommends monitoring levels of serum phosphorus and calcium. Patients receiving phosphate binders will have their phosphorus, calcium and parathyroid hormone levels measured at least quarterly at the hospital.
Lanthanum (generic)	Chewable tablets containing 500mg, 750mg or 1000mg lanthanum carbonate. Sachets containing 750mg and 1000mg lanthanum carbonate oral powder. Control of serum phosphate level has been demonstrated at doses starting from 750mg per day. The maximum dose studied in clinical trials, in a limited number of patients, was 3750mg. Patients who respond to lanthanum therapy usually achieve acceptable serum phosphate levels at doses of 1500mg to 3000mg lanthanum per day.	Lanthanum should be taken with or immediately after food, with the daily dose divided between phosphate-containing meals. Tablets must be chewed and not swallowed whole. 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, with regular monitoring thereafter. **Second-line phosphate binder therapy; used for patients intolerant of calcium-containing phosphate binders or those with baseline hypercalcaemia or who develop hypercalcaemia and/or suppressed PTH levels on calcium-containing binder therapy. May be used as a therapeutic switch for patients requiring high doses of sevelamer (9 tablets per day or more) to improve concordance and reduce pill burden.**	Clotting of the haemodialysis graft, myalgia and cough.	Lanthanum is contra-indicated in pregnancy.	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.	The SPC recommends monitoring levels of serum phosphorus and calcium. Patients receiving phosphate binders will have their phosphorus, calcium and parathyroid hormone levels measured at least quarterly in the hospital environment.

Phosphate binder	Dose	Comments	Adverse effects	Contraindications	Clinically significant drug interactions	Monitoring requirements
Sucroferric Oxyhydroxide (Velphoro®)	Available as chewable 500mg tablets. Tablets should be chewed and not swallowed whole. The recommended starting dose is 1500mg (3 tablets) per day, divided across the meals of the day. The dose can be increased to a maximum dose of 3000mg (6 tablets) per day, divided across the meals of the day. Most patients achieve optimal serum phosphorous levels at doses of 1500 to 2000mg per day.	Tablets can be crushed if the patient prefers not to chew tablets. **Second-line phosphate binder therapy; used for patients intolerant of calcium-containing phosphate binders or those with baseline hypercalcaemia or who develop hypercalcaemia and/or suppressed PTH levels on calcium-containing binder therapy. May be used as a therapeutic switch for patients requiring high doses of sevelamer (9 tablets per day or more) to improve concordance and reduce pill burden.**	Can discolour stools black. Other common adverse effects may include diarrhoea, nausea, constipation, vomiting, dyspepsia, abdominal pain, flatulence, tooth discolouration and abnormal taste.	Must not be used in patients with haemochromatosis or any other iron accumulation disorder.	Can reduce the absorption of tetracycline and quinolone antibiotics. If concurrent use can't be avoided, Velphoro® should be avoided 1 hour before and 2 hours after taking antibiotics. Velphoro® can theoretically reduce the absorption of levothyroxine. If patients use levothyroxine and require a dose of Velphoro® with their breakfast, additional monitoring of TFTs may be required following the initiation of treatment and/or any dose changes.	The SPC recommends monitoring levels of serum phosphorus and calcium. Patients receiving phosphate binders will have their phosphorus, calcium and parathyroid hormone levels measured at least quarterly in the hospital environment.