

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

- The request for shared care should include individual patient information, outlining all relevant aspects of the patients care and which includes direction to the information sheets at www.nottsapc.nhs.uk.
- If the GP does not agree to share care for the patient then he/she will inform the Specialist of his/her decision in writing within 14 days.
- In cases where shared care arrangements are not in place or where problems have arisen within the agreement and patient care may be affected, the responsibility for the patient's management including prescribing reverts 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, and these include calcium carbonate (Calcichew[®]), calcium acetate (Phosex[®] and Renacet[®]), sevelamer carbonate (generic) and lanthanum (Fosrenol[®]). These products may be used in combination with 1-hydroxycholecalciferol (alfacalcidol, One-Alpha[®]) or one of its analogues or cinacalcet (Mimpara[®]) to control the development of hyperparathyroidism and renal bone disease.

Calcium-based phosphate binders are generally used as the initial binder therapy for patients with chronic kidney disease as they are cheap and relatively efficacious, in conjunction with dietary phosphate restriction, to control phosphorus and parathyroid levels.

For patients with raised calcium levels, despite modifications in the dose of alfacalcidol and the use of cinacalcet, sevelamer or lanthanum (where tablet load with sevelamer is a problem) may be required, usually in addition to other therapies. They may also be required to improve patient concordance by reducing the tablet burden of other phosphate binders.

NATIONAL/ LOCAL GUIDANCE

NICE collaborating centre for Chronic Conditions. Clinical Guideline (24th September 2008) – Chronic Kidney Disease; Early identification and management in adults in primary and secondary care. Available from www.nice.org.uk/nicemedia/pdf/CG073FullGuideline.pdf

NICE. Management of hyperphosphataemia in Chronic Kidney Disease. Guideline 157. March 2013. Available from <http://www.nice.org.uk/nicemedia/live/14092/63034/63034.pdf>

Detailed guidelines exist within NUH for the management of bone and mineral metabolism in patients with CKD (attached). These include guidance on the use of oral phosphate binders, activated vitamin D compounds and 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 working diagnosis.
2. The specialist will recommend and initiate the treatment.
3. The specialist will ensure that the patient has an adequate supply of medication (usually 28 days) until shared care arrangements are in place. Further prescriptions will be issued if, for unseen reasons, arrangements for shared care are not in place at the end of 28 days. Patients should not be put in a position where they are unsure where to obtain supplies of their medication.
4. If shared care is considered appropriate for the patient, and the patient's treatment and condition are stable, the specialist will contact the GP.
5. 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 GP*
 - details of other treatments being received by the patient that are not included in shared care
 - details of monitoring arrangements

*Including reasons for choice of treatment, drug or drug combination, frequency of treatment, number of months of treatment to be given before review by the consultant.
6. Whenever the specialist sees the patient, he/she will
 - send a written summary within 14 days to the patient's GP.
 - record test results on the patient-held monitoring booklet if applicable
 - communicate any dosage changes made to the patient
7. The specialist team will be able to provide training for primary care prescribers if necessary to support the shared care agreement.
8. Contact details for primary care prescribers for during working and non working hours will be made available
9. Details for fast track referral back to secondary care will be supplied.
10. 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

The GP will be responsible for:

1. Ensuring that he/she has the information and knowledge to understand the therapeutic issues relating to the patients clinical condition.
2. Undergoing any additional training necessary in order to carry out a practice based service.
3. Agreeing that in his / her opinion the patient should receive shared care for the diagnosed condition unless good reasons exist for the management to remain within secondary care.
4. If the GP does not agree to shared care for the patient then he/ she will inform the Specialist of his/her decision in writing within 14 days.
5. Prescribing the maintenance therapy in accordance with the written instructions contained within the GP information sheets, and communicating any changes of dosage made in primary care to the patient. It is the responsibility of the prescriber that makes a dose change to communicate this to the patient.
6. Where applicable keep the patient-held monitoring booklet up to date with the results of investigations changes in dose and alterations in management and take any actions necessary. It is the responsibility of the clinician actioning the results from monitoring, in accordance with this shared care guideline, and thereby prescribing for the patient to complete the patients record with the necessary information.
7. Reporting any adverse effect in the treatment of the patient to the consultant.
8. The GP will ensure that the patient is monitored as outlined in the information sheet(s) and will take the advice of the referring consultant 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. 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 (attached). These include guidance on the use of oral phosphate binders, activated vitamin D levels and calcimimetics.

NICE collaborating centre for Chronic Conditions. Clinical Guideline (24th September 2008) – Chronic Kidney Disease; Early identification and management in adults in primary and secondary care. Available from www.nice.org.uk/nicemedia/pdf/CG073FullGuideline.pdf

ORIGINAL AUTHORS 2010

(This shared care protocol has been adapted from the Derbyshire Joint Area Prescribing Committee Shared Care Agreement for Phosphate Binders in the treatment of hyperphosphataemia in patients on dialysis.)

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IN CONSULTATION WITH

Consultant Nephrologists, Nottingham University Hospitals NHS Trust

2013 VERSION

Updated by Dr Simon Roe, Consultant Nephrologist, Nottingham University Hospitals NHS Trust.

Minor update August 2015 to change Phoslo[®] to Renacet[®] due to discontinuation in consultation with Dr Simon Roe and Ian Hogg (Renal Pharmacist, NUH). October 2016: Renvela to sevelamer carbonate (generic) following consultation with JFG and Ian Hogg.

Nottinghamshire Area Prescribing Committee

CONTACT DETAILS (In Hours and Out of Hours)

	Base	In hours contact	Out of hours contact
Dr Simon Roe, Consultant Nephrologist	City Hospital Campus, NUH	0115 9691169 Extn 54462	On Call Renal StR or consultant via NUH switchboard
Bruno Mafri, Specialist Renal Dietitian	City Hospital Campus	0115 9691169 Extn 55325	
Ian Hogg, Renal Pharmacist	City Hospital Campus	0115 9691169 Extn 55612	On-call pharmacist bleep via switchboard

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 (Fosrenol®) are all licensed as phosphate binding agents for the correction of hyperphosphataemia associated with chronic renal failure in patients undergoing dialysis.

Prescribing outside of licensed indication

Calcium Carbonate (Calcichew®), Calcium Acetate (Phosex®), Calcium Acetate (Renacet®), Sevelamer (Renagel®), Lanthanum (Fosrenol®) are not licensed for use in patients not undergoing dialysis. However, there is substantial experience of clinical use in this population.

Any exclusions 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 Registrar's in renal medicine, usually with input from specialist renal dieticians.

Products available

Calcium Carbonate (Calcichew®), Calcium Acetate (Phosex®), Calcium Acetate (Renacet®), Sevelamer carbonate (generic), Lanthanum (Fosrenol®)

Dosages and route of administration

See table

Duration of treatment

Life long

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.

Explicit criteria for review and discontinuation of the medicine

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
Calcium	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)
Phosphate	0.9–1.5 mmol/l Ideally within normal range	0.9–1.5 mmol/l Ideally within normal range	1.1–1.7 mmol/l Aim towards normal range
PTH	14-72 ng/l	144-648 ng/l ¹	144-648 ng/l ¹

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 or calcium containing phosphate binders Consider introduction of non-calcium containing phosphate binder

Contraindications See table overleaf.

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

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.

Phosphate binder	Dose	Comments	Adverse effects	Contraindications	Clinically significant drug interactions	Monitoring requirements
Calcium Carbonate (Calcichew®)	Chewable tablets containing 1.25g (calcium 500mg). Adults, children and elderly: Dose as required by the individual patient depending on serum phosphate level.	The tablets should be taken just before or during each meal. (NB not after meals) Tablets may be chewed or sucked	Hypercalcaemia and hypercalcuria. Constipation, flatulence, nausea, abdominal pain and diarrhoea.	Calcium salts are contra-indicated in hypercalcaemia and hypercalciuria Nephrolithiasis	The Summary of Product Characteristics (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 Summary Product Characteristics 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 1000 mg (calcium 250mg). An initial starting dose of three tablets daily, 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. Most patients need 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 first line phosphate binder. More effective than calcichew and less elemental calcium. Renacet is a small tablet and some patients find this easier to swallow than the large Phosex tablets. The elemental calcium content of Renacet is less than Phosex, therefore the number of capsules required per meal may be more with Renacet.	Hypercalcaemia and hypercalcuria. Constipation, flatulence, nausea, abdominal pain and diarrhoea.	Calcium salts are contra-indicated in hypercalcaemia and hypercalciuria		
Calcium Acetate (Renacet®) Phoslo® was discontinued May 2015	Tablets containing calcium acetate 475mg (calcium 120.25 mg). 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 3 to 4 tablets 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 on phosphate binders 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 their dietary advice. 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.	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 in the hospital environment.

Phosphate binder	Dose	Comments	Adverse effects	Contraindications	Clinically significant drug interactions	Monitoring requirements
Lanthanum (Fosrenol®)	Tablets containing 250mg, 500mg, 750mg or 1000 mg. Sachets containing 750mg and 1000mg lanthanum carbonate powder. 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	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	Clotting of the haemodialysis graft, myalgia and cough.	Lanthanum is contra-indicated in pregnancy	The Summary of Product Characteristics 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 Summary of Product Characteristics 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

	<p>patients, is 3750 mg. Patients who respond to lanthanum therapy usually achieve acceptable serum phosphate levels at doses of 1500mg to 3000mg lanthanum per day.</p>	<p>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.</p>				<p>hospital environment.</p>
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