Shared Care Guideline for Phosphate Binders in Hyperphosphataemia in Adults Patients with Chronic Kidney Disease (CKD)

Sevelamer Carbonate/Hydrochloride (phosphate binder). Lanthanum Carbonate (phosphate binder)

Executive Summary/ Critical Information.

Indication	Route & Dose	Key aims of treatment in the long term	Monitoring undertaken by specialist before requesting shared care	Ongoing monitoring to be undertaken by GP	Duration of treatment	Stopping criteria	Follow up (weeks/ months)
• Control of hyperphosphataemia in adult CKD patients receiving haemodialysis (HD) or peritoneal dialysis (PD). • Control of hyperphosphataemia in adult CKD (stage 4 or 5) patients not on dialysis, who cannot be prescribed calcium-based phosphate binders due to persistently raised corrected calcium levels or if serum parathyroid hormone levels are low. • Control of hyperphosphataemia in adult CKD (stage 4 or 5) patients, in addition to calcium-based phosphate binder if hyperphosphataemia persists. • Lanthanum is chosen if the patient is intoleratant of Sevelamer.	**Sevelamer:** Initiating dose is 800-1600mg three times a day with meals. **Lanthanum:** Initiating dose is 250mg three times a day with meals. See full details below.	Manage levels of phosphate and corrected calcium **Aim for phosphate level of 0.9-1.5mmol/L in CKD stage 4 or 5 (not on dialysis) or 1.1-1.7mmol/L on dialysis.**	Serum phosphate levels every 2-4 weeks Corrected calcium level every 2-4 weeks	Patient's overall health Adverse events Patient's compliance and tolerance with medication.	Ongoing according to serum phosphate and corrected calcium levels.	Intolerance to treatment Decision to stop medication should be made by specialist, and GP informed	**Specialist - Monthly - Quarterly**

Key Safety Notice (for instance: notification if prescribing must be brand specific or BNF cautionary and advisory warnings).

Other

This document has been produced in collaboration with the following organisations: Barts Health, NEL, Newham CCG, Tower Hamlets CCG, Waltham Forest CCG.

1. Background

Patients with CKD carry a higher risk of developing other severe co-morbidities such as hyperphosphataemia. Hyperphosphataemia occurs due to insufficient filtering of phosphate from the blood by poorly functioning kidneys and can lead to secondary hyperparathyroidism by increasing parathyroid hormone secretion. As a result, secondary parathyroid increases morbidity, mortality and renal bone disease if left untreated. Symptoms include bone and muscular pain, increased incidence of fracture, abnormalities of bone and joint morphology, vascular and soft tissue calcification, and cardiovascular disease.

Drugs used to treat the condition:

- Calcium-based phosphate binders such as Calcium acetate and Calcium carbonate
- Sevelamer
- Lanthanum

Phosphate binders are used to bind to phosphate, which can be obtained from the diet, in the gastro-intestinal tract and prevents it from being absorbed into the blood stream. It should be used within the context of a multiple therapeutic approach, which could include calcium supplements, 1,25-dihydroxy vitamin D3 or one of its analogues, to control the development of renal bone disease.

Sevelamer is particularly used in renal patients who cannot be prescribed calcium-based phosphate binders, due to persistently raised corrected calcium levels. Sevelamer may also be prescribed in addition to a calcium-based phosphate binder if hyperphosphataemia persists.

Lanthanum is reserved for use as an alternative to sevelamer as monotherapy where calcium containing binders cannot be prescribed due to contraindications or tolerability, in addition to calcium binders where despite reaching optimal dose the phosphate level is not adequately controlled, and where sevelamer has been tried but is ineffective or not tolerated.

2. Important information

Sevelamer; the available formulations are as tablets (sevelamer hydrochloride/carbonate) or powder (sevelamer carbonate)

Lanthanum; the available formulations are as tablets (Lanthanum carbonate) or powder (lanthanum carbonate)

3. Drug name, form, and licensed indications (unlicensed/off-label)

Drug Name	Form	Licensed Indications
Sevelamer Carbonate	**800mg film coated tablets.** **2.4g powder sachets**	Sevelamer carbonate is licensed for the control of hyperphosphataemia in adult patients on haemodialysis or peritoneal dialysis and in CKD patients not on dialysis, with a serum phosphate of concentration of 1.78mmol/L or more. Sevelamer carbonate contains the same active moiety as sevelamer hydrochloride but instead of hydrochloride contains a carbonate buffer and thus has a better GI tolerability than sevelamer hydrochloride.

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Sevelamer hydrochloride	800mg film coated tablets	Sevelamer hydrochloride is licensed for the treatment of hyperphosphataemia in patients on haemodialysis or peritoneal dialysis
Lanthanum carbonate	Chewable tablets containing 500mg, 750mg or 1g Powder sachets containing 750mg or 1g oral powder.	Lanthanum is licensed for the treatment of hyperphosphataemia in patients on haemodialysis or peritoneal dialysis and in CKD patients not on dialysis, with a serum phosphate of concentration of 1.78mmol/L or more

4. Dose and Administration

Drug	Dose
Sevelamer (Carbonate/Hydrochloride)	• Starting dose 800-1600mg (one-two tablets) three times a day, orally just before meals. The dose of sevelamer is then adjusted according to serum phosphate levels. Dosage may vary between one and five 800mg tablets per meal. The tablets should be swallowed whole. • Usual dose is 6g daily in three divided doses • Sevelamer carbonate powder for oral suspension is available in sachets containing 2.4g of sevelamer carbonate. The recommended staring dose is 2.4g or 4.8g based on clinical needs or serum phosphorus levels. In clinical practice, treatment will be continuous based on the need to control serum phosphorus levels and the daily dose is expected to be an average of approximately 6 g per day. • Sevelamer carbonate powder should be mixed with water before administration. Each sachet of 2.4 g of powder should be dispersed in 60 mL of water prior to administration The suspension should be ingested within 30 minutes after being prepared. As an alternative to water, the powder may be pre-mixed with a small amount of beverage or food (e.g. 100 grams/120 ml) and consumed within 30 minutes. Do not heat sevelamer carbonate powder (e.g. microwave) or add to heated foods or liquids.
Lanthanum Carbonate	• The starting dose is 750mg daily in divided doses with or immediately after meals and adjusted according to serum phosphate levels. The maximum licensed dose is 3750mg daily. • The usual dose range is 1.5-3g daily in divided doses. • Tablets must be chewed *thoroughly* to ensure maximum effectiveness. • Lanthanum® oral powder is intended to be mixed with a small quantity of soft food. Lanthanum® oral powder is insoluble and must not be dissolved in liquid for administration

5. Contraindications/Cautions

Drug	Contraindications	Cautions
Sevelamer (Carbonate/ Hydrochloride)	Hypophosphataemia Bowel obstruction.	Closer monitoring of patients with hypothyroidism co-administered with sevelamer carbonate and levothyroxine is recommended Caution in gastrointestinal disorders

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Lanthanum Carbonate	Hypophosphataemia	There have been cases of gastrointestinal obstruction, ileus, subileus, and gastrointestinal perforation reported in association with Lanthanum®.Exercise caution in all patients predisposed to gastrointestinal obstruction, ileus, subileus and perforation. Lanthanum® is known to cause constipation and therefore caution should be exercised in patients predisposed to bowel obstruction (e.g. previous abdominal surgery, peritonitis). Lanthanum® is not metabolised by liver enzymes but it is most likely excreted in the bile. Conditions resulting in a marked reduction of bile flow may be associated with incrementally slower elimination of Lanthanum® , which may result in higher plasma levels and increased tissue deposition of Lanthanum® As the liver is the principal organ of elimination of absorbed Lanthanum® monitoring of liver function tests is recommended on a quarterly basis

For complete list of contraindications and cautions, please refer to the SPC: https://www.medicines.org.uk/emc.

Pregnancy and Breastfeeding

Drug	Pregnancy	Breastfeeding
Sevelamer (Carbonate/Hydrochloride)	There are no data from the use of sevelamer in pregnant women. Studies in animals have shown some reproductive toxicity when sevelamer was administered to rats at high doses. Sevelamer has also been shown to reduce the absorption of several vitamins including folic acid. The potential risk to humans is unknown. Sevelamer should only be given to pregnant women if clearly needed and after a careful risk/benefit analysis has been conducted for both the mother and the foetus.	It is unknown whether sevelamer is excreted in human breast milk. The non-absorbed nature of sevelamer indicates that excretion of sevelamer in breast milk is unlikely. A decision on whether to continue/discontinue breast-feeding or to continue/discontinue therapy should be made taking into account the benefit of breast-feeding to the child and the benefit of therapy to the woman.
Lanthanum Carbonate	There are no adequate data from the use of Lanthanum® in pregnant women. Lanthanum® is not recommended for use during pregnancy.	It is unknown whether Lanthanum® is excreted in human breast milk. The excretion of Lanthanum® in milk has not been studied in animals. Caution should be used in taking a decision whether to continue/discontinue breast feeding or to continue/discontinue therapy with

		Lanthanum® , taking into account the potential benefit of breast feeding to the child and the potential benefit of Lanthanum® therapy to the nursing mother.

6. Drug interactions

Drug	Interactions
Sevelamer (Carbonate/Hydrochloride)	Sevelamer has no specific interactions information. However, drugs for which a reduction in bioavailability could be clinically important should be administered at least 1 hour before, or 3 hours after, sevelamer; alternatively consider monitoring blood concentrations. Examples of these drugs are: • Ciprofloxacin • Ciclosporin • Mycophenolate • Tacrolimus
Lanthanum Carbonate	Lanthanum may increase gastric pH. Certain drugs such as chloroquine, hydroxychloroquine and ketoconazole should not be taken within 2 hours of administration. The bioavailability of ciprofloxacin, tetracycline and doxycycline can be reduced by Lanthanum. It is recommended that these drugs should be taken at least 2 hours before or 4 hours after administration.

For complete list of drug interactions, please refer to the SPC: https://www.medicines.org.uk/emc.

7. Side effects which require managing

Sevelamer Carbonate/Hydrochloride

In very rare cases, intestinal obstruction and ileus/subileus have been observed in patients during treatment with sevelamer. Constipation may be a preceding symptom. Patients should be advised to inform their doctor or pharmacist if constipation occurs. Patients who are constipated should be monitored carefully and treatment reviewed in patients who develop severe constipation.

Adverse effects (Very common/ common)	Symptoms/signs	Actions
Gastrointestinal Disorders	Diarrhoea, nausea, vomiting, dyspepsia, constipation (most common) Flatulence (common) Abdominal pain.	Consider sevelamer carbonate if patient was taking sevelamer hydrochloride. **If patient is intolerant, seek advice from consultant as treatment may need to be stopped.**
Nervous system disorders	Headache, leg cramps, dizziness	**If patient is intolerant, seek advice from consultant as treatment may need to be stopped.**

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Lanthanum carbonate hydrate

Adverse effects (Very common/ common)	**Symptoms/signs**	**Actions**
Metabolism disorders	Hypocalcaemia	Add calcium/vitamin D supplement but monitor Corr Serum Ca^{2+} levels.
Gastrointestinal disorders	Abdominal pain, constipation, diarrhoea, dyspepsia, flatulence, nausea and vomiting	Check if patients take the tablets appropriately (e.g. chew tablets thoroughly and take with or immediately after meal) **If patient is intolerant, seek advice from consultant as treatment may need to be stopped.**
Nervous system disorders	Dizziness, headache, taste alteration	
Skin disorders	Pruritis, rash	

For complete list of side effects, please refer to the SPC: https://www.medicines.org.uk/emc.
Report any serious adverse drug reactions to the MHRA via the Yellow Card reporting mechanism https://yellowcard.mhra.gov.uk/yellowcards/reportmediator/

8. Process for Referral Back to Secondary Care

Patients who are not tolerating Sevelamer or Lanthanum please refer back to the referring consultant.

9. Monitoring and Responsibilities

a) Hospital Specialist

- Ensure that the patient/carer is an informed recipient in therapy.
- Ensure that patients understand their treatment regimen and any monitoring or follow up that is required (using advocacy if appropriate). Issue any local patient information leaflets where appropriate.
- Ensure baseline investigations are normal before commencing treatment.
- Initiate treatment and prescribe until the GP formally agrees to share care (as a minimum, supply the first month of treatment or until patient is stabilised).
- Send a letter to the GP requesting shared care for this patient.
- Clinical and laboratory supervision of the patient by blood monitoring and routine clinic follow-up on a regular basis.
- Send a letter/results notification to the GP after each clinic attendance ensuring current dose, most recent blood results and frequency of monitoring are stated.
- Where the GP is not performing the phlebotomy, the blood test form MUST be annotated to request that blood results are also copied to the GP

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- Evaluation of any reported adverse effects by GP or patient.
- Advise GP on review, duration or discontinuation of treatment where necessary. Where urgent action is required following tests the hospital team will telephone the patient and inform GP.
- Inform GP of patients who do not attend clinic appointments.
- Counsel the patient on contraception and what to do if pregnancy occurs. Document in the notes.
- Ensure that backup advice is available at all times.
- Ensure that the patient has received a flu vaccine prior to commencing treatment that is likely to cause immunosuppression. Document this in the patient notes and inform the GP it has been given

b) General Practitioner

- Reply to the request for shared care as soon as practical (within 14 days) particularly if you are unable to accept the shared care agreement stating the reason(s) why.
- Prescribe the drug treatment in accordance with the specialist's recommendation
- Ensure that patients understand their treatment regimen and any monitoring or follow up that is required (using advocacy if appropriate).Contact the specialist for clarification where appropriate.
- Monitor patient's overall health and well-being.
- Report any adverse events to the consultant, where appropriate.
- Report any adverse events to the CSM, where appropriate.
- Help in monitoring the progression of disease

c) Clinical Commissioning Group (CCG)

Who may delegate this task to the Commissioning Support Unit (CSU)

- To provide feedback to trusts via Trust Medicines Committee.
- To support GPs to make the decision whether or not to accept clinical responsibility for prescribing.
- To support trusts in resolving issues that may arise as a result of shared care.

d) Patient/ Carer

- Report any adverse effects to their GP and/or specialist
- Ensure they have a clear understanding of their treatment.
- Report any changes in disease symptoms to GP and/or specialist
- Alert GP and/or specialist of any changes of circumstance which could affect management of disease e.g. plans for pregnancy
- Take/ administer the medication as prescribed
- Undertake any monitoring as requested by the GP and/or specialist

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10. Contact Information

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Renal Specialist Pharmacist	0203 246 0134 (Direct Line)
Medicines Information Pharmacist	0208 535 6971 (Direct Line)

11. References

1) NICE Guidance CG157: Chronic kidney disease (stage 4 or 5): Management of hyperphosphataemia https://www.nice.org.uk/guidance/cg157/chapter/1-Recommendations#phosphate-binders-children-young-people-and-adults

2) Summary of Product Characteristics for Sevelamer https://www.medicines.org.uk/emc/product/472/smpc

3) British National Formulary for Sevelamer https://www.formularycomplete.com/view/drug/monograph/89155

12. Document Management

Document ratification and history	
Produced by:	Barts Health, WEL CCGs
Approved by:	Waltham Forest and East London Medicines Optimisation and Commissioning Committee (WELMOCC)
Date approved:	28/04/2021
Ratified by:	Barts Health Drugs and Therapeutics Committee
Date ratified:	05/05/2021
Review date:	3 years - or sooner if evidence or practice changes
Obsolete date:	April 2024
Version number:	1

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Appendix 1.

Shared Care Guideline: Prescribing Agreement

Section A: To be completed by the hospital consultant initiating the treatment

GP Practice Details:	**Patient Details:**
Name:	Name:
Tel No:	DOB:
Email (nhs.net):	NHS Number (10 digits):

Consultant Details:
Consultant Name:
Secretary Contact Details:
Tel No:
Email (nhs.net):

Diagnosis:	**Drug Name (to be prescribed by GP):** **Dose:** **Frequency:**

I will review the patient in clinic in weeks / months (*Delete as appropriate)*.

Dear

Your patient started treatment with the above drug for the above diagnosis on (insert date) and in my view; his/her condition is now stable.

The patient has given consent to treatment under a shared care prescribing agreement and has agreed to comply with instructions and follow up requirements.

I am requesting your agreement to sharing the care of this patient from (insert date) in accordance with the attached Shared Care Prescribing Guideline.
This patient was reviewed on (insert date). These are the results relevant for the drug and/or condition, as outlined in the shared care document:

Test	Baseline	Date

Please continue to monitor the patient as outlined in the shared care guidelines. Refer to the attached guidelines for monitoring criteria.

Other relevant information:

Consultant Signature:	Date:

Section B: To be completed by the GP and returned to the hospital consultant as detailed in Section A above [If returned via e-mail, use NHS.net email account ONLY]

Please sign and return your agreement to shared care within 14 days of receiving this request.

☐ Yes, I accept sharing care as per shared care prescribing guideline.

☐ No, I am not willing to undertake shared care for this patient for the following reason:

(Please give reason)

GP Name:	GP Signature:	Date:

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