

**MANAGEMENT OF HYPERPHOSPHATAEMIA  
AND SECONDARY  
HYPERPARATHYROIDISM IN CHRONIC  
KIDNEY DISEASE – MINERAL BONE  
DISORDER (CKD-MBD)**

**1. Introduction and Who Guideline applies to**

This guideline should be used to treat hyperphosphataemia and secondary hyperparathyroidism (SHPT) in patients with chronic kidney disease (CKD) (all stages including those requiring dialysis). It is for use by doctors, other qualified prescribers and staff acting under a patient group direction (PGD).

Clinical guidelines are ‘guidelines’ only. The interpretation and application of clinical guidelines will remain the responsibility of the individual practitioner. If in doubt consult a senior colleague or expert.

This guideline should be used in conjunction with the Renal Association (2018) Commentary on the KDIGO Guideline on the Diagnosis, Evaluation, Prevention and Treatment of CKD-MBD <https://renal.org/wp-content/uploads/2018/06/FINAL-KDIGO-CKD-MBD-commentary-Final-for-publication.pdf>

***NB. There are no longer specific target ranges for serum phosphate, serum calcium and serum parathyroid hormone (PTH) levels for people with CKD. Local normal ranges should be used.***

KDIGO 2017 Clinical Practice Guideline Update for the Diagnosis, Evaluation, Prevention, and Treatment of Chronic Kidney Disease–Mineral and Bone Disorder (CKD-MBD) <https://kdigo.org/wp-content/uploads/2017/02/2017-KDIGO-CKD-MBD-GL-Update.pdf>

**2. Guideline Standards and Procedures**

**HYPERPHOSPHATAEMIA**

Aim for phosphate reduction towards normal in those with progressively rising or persistently elevated serum phosphate (not pre-emptively)

**Summary of recommendations**

- Limit dietary phosphate intake – Renal Dietitians to advise
- Use phosphate binders
- Limit the use of calcium based phosphate binders – they are no longer considered a clear first line choice
- Avoid hypercalcaemia

**Summary of phosphate binders**

<i>Generic name</i>	<i>Trade name</i>	<i>Dosage</i>	<i>Elemental Ca<sup>2+</sup> per tablet</i>	<i>NHS Cost per tablet / sachet</i>	<i>Instructions</i>	<i>Comments</i>
Calcium carbonate	Adcal	1.5g	600mg	9p	Chew before food	Each tablet equivalent binding capacity except 475mg Renacet. Smaller so
Calcium carbonate	Calcichew	1.25g	500mg	9p	Chew before food	
Calcium acetate	Renacet	475/950mg	120/241mg	5p / 9p	Swallow	

	Phosex	1g	250mg	11p	with food	easier to swallow but will need double the dose. All much cheaper than non-calcium containing alternatives <u>except generic Sevelamer</u>
Calcium acetate and magnesium carbonate	OsvaRen	435mg calcium acetate & 235mg magnesium carbonate	110mg (60mg magnesium)	13p	Swallow with food	
Sevelamer carbonate	Generic	800mg	None	17p	Swallow with food	Likely to need in large quantities to achieve control. NB Lower cost of generic sevelamer carbonate
Sevelamer hydrochloride / carbonate	Renagel /Renvela	800mg (powder is 2.4g)	None	93p (£2.78)	Swallow with food (mix with water and take with meals)	
Lanthanum carbonate	Fosrenol	500mg 750mg 1g (powder sachet in 750mg & 1g)	None	£1.38 £2.03 £2.15 (£2.03 & £2.15)	Chew <b>after</b> food (can sprinkle powder on/in food)	Available in different strengths so can increase dose within same amount of tablets/sachets
Sucroferric oxyhydroxide	Velphoro	500mg	None	£1.99	Chew with food	Max 3g / day. May cause discoloured faeces and transient diarrhoea
Aluminium hydroxide	Alu-caps	475mg	None	11p	Swallow with food	Rarely used

#### Considerations when prescribing phosphate binders

- Check Proton to assess current prescribing of binders and alfacalcidol
- Cross-check these details with patient and check compliance
- Check to see if previous binders have been tried and tolerated
- Calcium vs non-calcium based
  - o Risk of hypercalcaemia (Review serum calcium level. Starting a calcium based binder with a serum calcium of  $\geq 2.40$ mmol/l is likely to cause hypercalcaemia)
  - o Risk of calcification
    - Potentially lower risk of calcification with non-calcium based binders
    - Calcium acetate (Renacet / Phosex) and calcium acetate with magnesium (Osvaren) will raise calcium levels less than calcium carbonate (Adcal / Calcichew) due to lower calcium content
- Cost

- Calcium based binders are all cheaper than non-calcium based binders with the exception of Sevelamer carbonate (generic)
- Ability to swallow tablets
- Patient preference

**Based on these factors, calcium acetate and sevelamer carbonate should be considered as first - line binders depending on whether calcium or non-calcium based binder appropriate.**

## **SECONDARY HYPERPARATHYROIDISM**

Treat PTH levels that are progressively rising or persistently above the upper normal limit for PTH in those with CKD3a-5 (not on dialysis). For those on dialysis, aim for levels in the range of 2-9 times the upper limit of normal. Avoid PTH levels below the lower normal limit due to treatment. (NB Check low PTH levels are not as a result of parathyroidectomy).

### **Summary of recommendations**

- Evaluate modifiable factors such as hyperphosphataemia, hypocalcaemia, high phosphate intake and vitamin D deficiency Use alfacalcidol in CKD 4-5 only in those with severe and progressive hyperparathyroidism.
- In those on dialysis, vitamin D analogues and calcimimetics are both considered acceptable treatment options.
- Individualise treatment
- Review current medication - phosphate binders, alfacalcidol, vitamin D supplementation. Altering any of these medications is likely to impact other CKD-MBD variables so ensure all variables are considered together.
- Consider parathyroidectomy for those that fail to respond to medical or pharmacological therapy

### **Alfacalcidol**

Alfacalcidol is an active form of vitamin D (does not require renal hydroxylation) used to increase serum calcium levels to suppress PTH – increases gastrointestinal (GI) absorption, increases osteoclastic resorption and increases renal reabsorption. GI phosphate absorption is also increased so alfacalcidol should not be started / increased if phosphate levels are high. Hypercalcaemia should be avoided. Recent practice has changed to avoid raising calcium levels unnecessarily (to the top of the normal range) thereby avoiding calcium loading of patients.

Start with 0.25micrograms of alfacalcidol once a day and adjust as necessary aiming to maintain serum calcium levels in the normal range.

NB. When making adjustments consider serum calcium, serum phosphate and serum PTH levels together. Monitor serum calcium level and PTH level at every routine outpatient visit (at least every three months)

### **Calcimimetics**

2 calcimimetics are available for use in dialysis patients – Cinacalcet tablets taken daily (Mimpara) for use in haemodialysis (HD) and peritoneal dialysis (PD) and Etelcalcetide injection (Parsabiv) which is given into the venous line of the dialysis circuit for those on HD. They work by acting on the calcium-sensing receptor to increase its sensitivity to calcium thereby reducing PTH secretion. Calcium levels will also fall and need to be monitored closely.

Medication	Cinacalcet	Etelcalcetide
Formulation	Tablet 30mg tablet, 60mg tablet, 90mg tablet	Bolus injection 2.5mg in 0.5ml solution, 5mg in 1ml solution, 10mg in 2ml solution
Cost per dose	30mg tablet - £4.49 60mg tablet - £8.28 90mg tablet - £12.43	2.5mg in 0.5ml solution - £22.81 5mg in 1 ml solution - £27.32 10mg in 2ml solution - £54.64
Starting dose	30mg once per day Serum calcium should be at or above the lower limit of normal range prior to administration.	5mg 3 times per week Serum calcium should be at or above the lower limit of normal range prior to administration. It should not be given more than three times per week.
Monitoring requirement	Serum calcium should be monitored within 1 week of initiation or dose adjustment and thereafter monthly PTH should be measured 1 to 4 weeks after initiation or dose adjustment. PTH levels should be assessed at least 12 hours after dosing with Cinacalcet	Serum calcium should be monitored within 1 week of initiation or dose adjustment and thereafter monthly PTH should be measured 4 weeks after initiation or dose adjustment.
Titrating	Can be titrated every 2 – 4 weeks to a maximum dose of 180mg once per day.	Can be titrated no more than every 4 weeks to a maximum dose of 15mg 3 times per week
Maintenance	Measure serum calcium monthly Measure PTH every 1-3 months	Measure serum calcium monthly Measure PTH every 1-3 months

N.B. Calcium levels may fall on treatment with calcimimetics. If serum calcium is low then follow guidance as below

### *Cinacalcet*

Corrected serum calcium or clinical symptoms of hypocalcaemia	Recommendations
< 2.1mmol/l and > 1.9mmol/l, or in presence of clinical symptoms of hypocalcaemia	Calcium-containing phosphate binders, vitamin D sterols and/or adjustment of dialysis fluid calcium concentrations can be used to raise serum calcium according to clinical judgement

< 2.1mmol/l and > 1.9mmol/l, or persistent symptoms of hypocalcaemia despite attempts to increase serum calcium	Reduce or withhold dose of Mimpara
≤ 1.9mmol/l or persistent symptoms of hypocalcaemia and vitamin D cannot be increased	Withhold administration of Cinacalcet until serum calcium levels reach 2.0mmol/l and/or symptoms of hypocalcaemia have resolved.  Treatment should be reinstated using the next lowest dose of Cinacalcet

### *Etelcalcetide*

Corrected serum calcium or clinical symptoms of hypocalcaemia	Recommendations
<2.08mmol/l and ≥ 1.88mmol/l	If clinically indicated - start or increase calcium supplements, calcium-containing phosphate binders, and/or vitamin D sterols - increase dialysate concentration - consider reducing Etelcalcetide dose
<1.88mmol/l	Stop Etelcalcetide until corrected serum calcium levels are ≥2.08mmol/l and symptoms of hypocalcaemia (if present) have resolved.  If clinically indicated - start or increase calcium supplements, calcium-containing phosphate binders, and/or vitamin D sterols - increase dialysate concentration - Reinitiate Etelcalcetide at a dose 5mg lower than the last administered dose. If patients last administered dose was 2.5mg or 5mg, reinstate at 2.5mg once corrected serum calcium levels are >2.08mmol/l and symptoms of hypocalcaemia (if present) have resolved.

### **3. Education and Training**

No new skills are required for implementing this policy. It will be uploaded onto the Policies and Guidelines Library to replace a previous version.

### **4. Monitoring Compliance**

What will be measured to monitor compliance	How will compliance be monitored	Monitoring Lead	Frequency	Reporting arrangements
Serum calcium levels	% adult CKD G5D with serum calcium above the normal reference range as reported to the Renal Registry	Richard Baines	Annually	Cascaded via email

### **5. Supporting References (maximum of 3)**

KDIGO (2017). *Clinical Practice Guideline Update for the Diagnosis, Evaluation, Prevention, and Treatment of Chronic Kidney Disease–Mineral and Bone Disorder (CKD-MBD)*. [Online]

Available at: <https://kdigo.org/wp-content/uploads/2017/02/2017-KDIGO-CKD-MBD-GL-Update.pdf>  
[Accessed 3 January 2019].

Renal Association (2018) *Commentary on the KDIGO guideline on the Diagnosis, Evaluation, Prevention and Treatment of CKD-MBD*. [Online]

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[Accessed 3 January 2019].

## **6. Key Words**

Hyperphosphataemia, secondary hyperparathyroidism, phosphate binders, CKD-MBD, calcium, phosphate, parathyroid hormone, calcimimetic

<b>CONTACT AND REVIEW DETAILS</b>	
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<b>Details of Changes made during review:</b> No changes.	