Shared Care Guideline for Refractory Secondary Hyperparathyroidism (SHPT) in adult patients with End Stage Renal Disease (ESRD)

Cinacalcet (calcimimetic)

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)
Treatment of refractory SHPT in patients with ESRD (including calciphylaxis) and on haemodialysis or peritoneal dialysis. Treatment is only for those: • With 'very uncontrolled' plasma levels of intact PTH (>85pmol/L [800pg/ml]) and a normal or high adjusted serum calcium level, **and** • Where surgical parathyroidectomy is contraindicated (i.e. risk of surgery outweighs the benefit)	Initiating dose is 30mg once a day, titrated every 2–4 weeks to a maximum of 180 mg once daily.	Manage levels of PTH, phosphate and calcium **A target level of intact PTH of between 15.9 and 31.8 pmol/L (150–300 pg/ml) should be achieved.**	PTH levels (aim for fall of PTH >30% of baseline) Serum phosphate levels Corrected calcium levels	Patient's overall health Adverse events Patient's compliance and tolerance with medication	Ongoing according to serum PTH, phosphate and corrected calcium levels.	Discontinue if PTH fall is <30% of baseline after four months of treatment (with maximum tolerated dose). Decision to stop medication should be made by specialist, and GP informed.	**Specialist - once/month**

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

Other

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1. Background

The parathyroid glands normally produce PTH, which controls the levels of calcium in the blood.
With renal function impairment, excess amounts of PTH are produced due to impaired excretion of phosphate, impaired reabsorption of calcium and reduced hydroxylation of inactive forms of vitamin D to the active form. This condition is called secondary hyperparathyroidism.

Cinacalcet is licensed for the treatment of SHPT in patients with ESRD on maintenance dialysis therapy, for prescribing as part of a therapeutic regimen including phosphate binders and/or vitamin D sterols as appropriate. Cinacalcet is described as a calcimimetic because it mimics the action of calcium, and can bind and activate the calcium receptors on parathyroid cells, thus suppressing the production of PTH.

Cinacalcet is initiated by the Renal Unit in accordance with NICE TA 117 criteria as follows:

- Cinacalcet is not recommended for the routine treatment of secondary hyperparathyroidism in patients with end-stage renal disease on maintenance dialysis therapy.
- Cinacalcet is recommended for the treatment of refractory secondary hyperparathyroidism in patients with end-stage renal disease (including those with calciphylaxis) only in those:
    - who have 'very uncontrolled' plasma levels of intact parathyroid hormone (defined as greater than 85 pmol/litre [800 pg/ml]) that are refractory to standard therapy, and a normal or high adjusted serum calcium level, **and**
    - in whom surgical parathyroidectomy is contraindicated, in that the risks of surgery are considered to outweigh the benefits.
- Response to treatment should be monitored regularly and treatment should be continued only if a reduction in the plasma levels of intact parathyroid hormone of 30% or more is seen within 4 months of treatment, including dose escalation as appropriate.

At Bart's Health all patients will have their Vitamin D analogues and phosphate binders titrated to the maximum tolerated dose, and their dialysis regimen modified where appropriate, before cinacalcet is considered.

This Shared Care Guidance is only applicable after the patient has been cared for solely by the Renal Unit for the first four months of therapy, with the Renal Unit doing all the prescribing and monitoring. Treatment will only be continued after 4 months if there has been 'treatment success'. All patients will be assessed for clinical outcome by the Renal Unit after 4 months treatment and a decision made regarding continuation. Treatment failure' is classified (as per NICE guidance) as a fall in PTH less than 30% of baseline, after four months treatment with the maximum tolerated dose. Therefore, if 'treatment failure' has occurred, cinacalcet therapy will be discontinued.

All patients who receive cinacalcet therapy after four months, will be jointly cared for by the Renal Unit and the GP, as per the Shared Care agreement.

2. Important information

Cinacalcet is not recommended for routine treatment of SHPT.
The available formulations are as tablets.

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

Cinacalcet (tablet) is a calcimimetic agent, which increases the sensitivity of calcium-sensing receptors to extracellular calcium ions. As a result, PTH release is inhibited. It may be used concomitantly with phosphate binders and/or vitamin D sterols as clinically appropriate.

Cinacalcet is licensed for the treatment of:

- Secondary hyperparathyroidism in patients with end-stage renal disease on dialysis
- Hypercalcaemia in parathyroid carcinoma; primary hyperparathyroidism

Cinacalcet is available as 30mg, 60mg and 90mg tablets.

4. **Dose and Administration**

- Starting dose 30mg tablet once a day, orally.
- Maximum dose increase of 30mg, no more than every 2 weeks.
- Dose should be increased if the drop in PTH is < 30% of baseline (assuming serum corrected calcium and phosphate are in the normal range)
- Up to a maximum dose of 180mg once a day
- Once PTH has fallen to 15.9-31.8 pmol/l (target range), remain on the same dose (assuming serum corrected calcium and phosphate are in the normal range)
- If PTH falls to < 15.9 pmol/l, reduce dose by 30mg (or stop if prescribed 30mg od)
- The dose is best taken once daily with food, though based on practical experience, we have seen a few patients experiencing adverse effects such as nausea, who benefited from splitting the dose to twice daily (particularly when high doses are prescribed).

Parameter	**Parathyroid hormone (PTH)**	**Serum phosphate**	**Serum corrected calcium**
Target level	15.9 – 31.8 pmol/L	<1.8 mmol/L	2.20 – 2.65 mmol/L
Frequency of monitoring	Fortnightly or monthly until maintenance dose established, then every 2 months where appropriate	Monthly	Monthly

5. **Contraindications/Cautions**

Cinacalcet is contraindicated in patients with a serum calcium level below the lower limit of the normal range (i.e. adjusted calcium level < 2.2mmol/L).

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

Pregnancy and lactation

The safety of cinacalcet has not been established in pregnant or lactating women.

Cinacalcet should be used during pregnancy only if the potential benefit justifies the potential risk to the foetus. Following careful benefit/risk assessment, a decision should be made to discontinue either breast-feeding or treatment with cinacalcet.

6. **Drug interactions**

- Medicinal products known to reduce serum calcium
- Patients receiving cinacalcet should not be given etelcalcetide

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- Cinacalcet may increase concentration of tacrolimus. In this case, tacrolimus levels should be monitored and dose adjusted accordingly by the renal specialist.

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

7. Side effects which require managing

Cinacalcet has a good safety profile, with the most widely reported adverse events being nausea and vomiting, which are generally mild/moderate in severity and transient in nature in the majority of patients. In practice, such adverse events have been more widely attributed to higher doses.

Adverse effects (Common/very common)	**Symptoms/signs**	**Actions**
Gastro-intestinal disorders	Nausea and vomiting Diarrhoea Non-cardiac chest pain	Consider splitting of dose or reducing dose where appropriate Stop if patient intolerant of adverse effects
Nervous system disorders	Dizziness Paraesthesia/tingling, seizures	Stop if patient intolerant of adverse effects
Skin and subcutaneous tissue disorders	Rash	Stop if patient intolerant of adverse effects, and effect not transient
Musculoskeletal, connective tissue and bone disorders	Myalgia	Stop if patient intolerant of adverse effects
Other	Hypocalcaemia (CorCa ,< 2.0mmol/l) Symptoms/signs :- Muscle spasm/twitching, paraesthesia/ tingling/ pins and needles, seizures	Consider reducing dose where appropriate Stop treatment if symptoms/signs present
Metabolism and Nutrition disorders	Weight loss, decreased appetite	Stop if patient intolerant of adverse effects/ if problem persists, and direct causal link probable

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 cinacalcet, please refer back to the referring consultant.

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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. Give the patient a patient held booklet for result monitoring if appropriate.
- 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
- 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.

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.
- Supporting GPs on decisions to accept clinical responsibility for prescribing or not.
- 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

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- 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

10. Contact Information

Barts Health NHS Trust	
Dr Andi Cove-Smith: a.cove-smith@nhs.net Dr Suzanne Forbes: suzanne.forbes2@nhs.net Dr Tom Oates: thomas.oates1@nhs.net Dr Ulla Hemmila: ulla.hemmila@nhs.net Dr Mark Blunden mblunden@nhs.net Dr Kate Wiles kate.wiles@nhs.net Dr Will White william.white9@nhs.net Dr Anila Laurence anila.laurence@nhs.net Dr Ravi Rajakariar) ravindra.rajakariar@nhs.net	Dr Omer Ali omer.ali@nhs.net Dr Saurabh Chaudhri saurabhchaudhri@nhs.net Dr Gavin Dreyer g.dreyer@nhs.net Dr Ajith James ajith.james1@nhs.net Dr Viayaasan Mahalingasivam: viyaasan.mahalingasivam@nhs.net Dr Nasreen Samad: n.samad@nhs.net Dr John Booth john.booth2@nhs.net Dr Sajeda Youssouf sajeda.youssouf@nhs.net Dr Stan Fan f.stanley@nhs.net
Renal Specialist Pharmacist	0203 246 0134 (Direct Line)
Medicines Information Pharmacist	0208 535 6971 (Direct Line)

11. References

1) NICE technology appraisal TA117: Cinacalcet for the treatment of secondary hyperparathyroidism in patients with end-stage renal disease on maintenance dialysis therapy https://www.nice.org.uk/guidance/ta117/chapter/5-Implementation

2) Summary of Product Characteristics for Cinacalcet https://www.medicines.org.uk/emc/product/11483/smpc

3) Stockley's Drug Interactions www.medicinescomplete.com

12. Document Management

Document ratification and history	
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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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