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SCP for Cinacalcet in PHPT	Dr S Muniyappa & Dr A Ahmed	1	March 2023	March 2026

Shared Care Protocol for Cinacalcet in Primary Hyperparathyroidism

Specialist responsibilities

- Assess the patient and provide diagnosis; ensure that this diagnosis is within scope of this shared care protocol (section 2) and communicated to primary care.
- Use a shared decision-making approach; discuss the benefits and risks of the treatment with the patient and/or their carer and provide the appropriate counselling (see section 11) to enable the patient to reach an informed decision. Obtain and document patient consent. Provide an appropriate patient information leaflet.
- Assess for contraindications and cautions (see section 4) and interactions (see section 7).
- Conduct required baseline investigations and initial monitoring (see section 8).
- Initiate and optimise treatment as outlined in section 5. Prescribe the maintenance treatment for at least 4 weeks and until optimised.
- Once treatment is optimised, complete the shared care documentation and send to patient's GP practice detailing the diagnosis, current and ongoing dose, any relevant test results and when the next monitoring is required. Include contact information (section 13).
- Prescribe sufficient medication to enable transfer to primary care, including where there are unforeseen delays to transfer of care.
- Conduct the scheduled reviews and monitoring in section 8 and communicate the results to primary care. After each review, advise primary care whether treatment should be continued, confirm the ongoing dose, and whether the ongoing monitoring outlined in section 9 remains appropriate.
- Reassume prescribing responsibilities if a woman becomes or wishes to become pregnant.
- Provide advice to primary care on the management of adverse effects if required.

Primary care responsibilities

- Respond to the request from the specialist for shared care in writing. It is asked that this be undertaken within 14 days of the request being made, where possible.
- If accepted, prescribe ongoing treatment as detailed in the specialists request and as per section 5, taking into any account potential drug interactions in section 7.
- Adjust the dose of Cinacalcet prescribed as advised by the specialist.
- Conduct the required monitoring as outlined in section 9. Communicate any abnormal results to the specialist.
- Manage adverse effects as detailed in section 10 and discuss with specialist team when required.
- Stop Cinacalcet and recheck bloods to restart with a lower dose of Cinacalcet if adjusted calcium is less than 2.20mmol/l; discuss with the specialist.
- Check compliance and increase Cinacalcet dose by 30mg if adjusted calcium is persistently (4 to 6 weeks) greater than 2.6; discuss with the specialist if dose greater than 60mg BD required (rare).
- Stop treatment as advised by the specialist.
- Refer the management back to the specialist if the patient becomes or plans to become pregnant.

Patient and/or carer responsibilities

- Take Cinacalcet as prescribed and avoid abrupt withdrawal unless advised by the primary care prescriber or specialist.

- Attend regularly for monitoring and review appointments with primary care and specialist, and keep contact details up to date with both prescribers. Be aware that medicines may be stopped if they do not attend.
- Report adverse effects to their primary care prescriber. Seek immediate medical attention if they develop any symptoms as detailed in section 11.
- Report the use of any over the counter medications to their primary care prescriber and be aware they should discuss the use of Cinacalcet with their pharmacist before purchasing any OTC medicines.
- Patients of childbearing potential should take a pregnancy test if they think they could be pregnant, and inform the specialist or GP immediately if they become pregnant or wish to become pregnant.

1. Background

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Cinacalcet is a calcimimetic which increases calcium sensor receptor sensitivity to extracellular calcium resulting in reduced secretion of parathyroid hormone (PTH). It is licenced to use in secondary hyperparathyroidism and in parathyroid malignancy for a while now. And it is only the calcimimetic licenced for its use in UK. After review of new data of cinacalcet use in primary hyperparathyroidism (PHPT), NICE has approved use in primary hyperparathyroidism in its latest guidelines on primary hyperparathyroidism available via: https://www.nice.org.uk/guidance/ng132.

Primary hyperparathyroidism patients will have elevated serum PTH and serum adjusted calcium which is responsible for the symptoms of PHPT and end-organ damage particularly causing renal effects like renal stones, nephrocalcinosis and or kidney injury, and on the bone causing osteoporosis and or fragility fracture.

Parathyroidectomy remains first line and definitive treatment option in patients with primary hyperparathyroidism where it is required. This will eliminate symptoms of hypercalcaemia and as well as end-organ effect on the kidneys and bone. Not all patients with primary hyperparathyroidism require surgical intervention. They can be treated conservatively by active monitoring of serum calcium on regular basis.

A. Primary hyperparathyroidism treated with non-surgical and non-Calcimimetics pathway in following set of patients with PHPT.

	Clinical scenario	Serum Adj. Calcium	Serum PTH
1	If patients have asymptomatic hypercalcaemia and no end organ effect on kidney and bone	<2.85mmol/l	PTH remains elevated or high normal (>4.6nmol/L

B. Primary hyperparathyroidism treated with surgical and non-Calcimimetics pathway in following clinical situations

	Clinical scenario	Serum Adj. Calcium	Serum PTH
1	If patients have osmotic symptoms with fragility fracture and or osteoporosis and or renal effect like renal stone or kidney injury	>2.60	Elevated
2	If patients with or without osmotic symptoms with fragility fracture and or osteoporosis and or renal effect (renal stone or kidney injury)	>2.85mmol/L	Elevated
3	If patients with or without osmotic symptoms and with or without fragility fracture and or osteoporosis and or renal effect (renal stone or kidney injury)	>3.00mmol/L	Elevated

C. Primary hyperparathyroidism: Not suitable for surgical intervention or failed surgical intervention; start on Calcimimetics if tolerated.

	Clinical situation where cinacalcet is recommended	Serum adjusted calcium	Serum PTH
1	Patients not suitable for parathyroid surgery due to comorbidity with symptoms of hypercalcaemia	>2.85mmol/L	Elevated
2	Failed parathyroid surgery after MDT review and or parathyroid exploration surgery	>2.85mmol/L	Elevated
3	Patients not suitable for parathyroid surgery due to comorbidity with or with without symptoms of hypercalcaemia	>3.00mmol/L	Elevated

This pharmacological approach treating PHPT with cinacalcet should be reserved for those patients in whom it is desirable to lower the serum calcium, increase BMD or both. For the control of hypercalcemia, cinacalcet is the treatment of choice. Cinacalcet reduces serum calcium concentrations to normal in many cases, but has only a modest effect on serum PTH levels. However, bone mineral density (BMD) does not change. To improve BMD, bisphosphonate therapy is recommended. Bisphosphonates improves BMD at the lumbar spine without altering the serum calcium concentration.

Patients on cinacalcet need to be followed up in secondary care and prescription could be taken over by primary care after stabilising serum calcium and when patient has definitive treatment plan about primary hyperparathyroidism.

Cinacalcet treatment is not alternative to parathyroidectomy, which is definitive treatment. It is now a licenced treatment for primary hyperparathyroidism:

1. It will help to alleviate symptoms of hypercalcaemia.
2. It does have effect of hyperparathyroidism on bone and kidneys. These patients will develop complications of primary hyperparathyroidism. This should be made clear to the patients.
3. Some patients do not tolerate cinacalcet. The most commonly reported side effects of cinacalcet are joint and muscle pain, diarrhoea, nausea, and respiratory infection, hypocalcaemia, and hypomagnesemia. Hence it will need regular monitoring of blood tests. Please refer BNF for other side effects.
4. Investigations needed to be done while on cinacalcet – see section 8

2. Indications

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Primary Hyperparathyroidism

3. Locally agreed off-label use

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n/a

4. Contraindications and cautions

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This information does not replace the Summary of Product Characteristics (SPC), and should be read in conjunction with it. Please see BNF & SPC for comprehensive information.

Contraindications:

- Hypersensitivity to the active substance/excipients

- Hypocalcaemia (see sections above for monitoring/management)

Cautions:

- QT prolongation, particularly in those already taking medicines that prolong the QT interval.
- Moderate to severe renal impairment
- Seizures – threshold lowered by significant reductions in serum calcium levels; closely monitor in patients receiving cinacalcet, particularly in patients with a history of a seizure disorder.
- Hypotension and/or worsening heart failure have been reported in patients with impaired cardiac function, in which a causal relationship to cinacalcet could not be completely excluded and may be mediated by reductions in serum calcium levels.

5. Initiation and ongoing dose regime

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- Transfer of monitoring and prescribing to primary care is normally after the patient's dose has been optimised and with satisfactory investigation results for at least 4 weeks.
- The duration of treatment & frequency of review will be determined by the specialist, based on clinical response and tolerability.
- All dose or formulation adjustments will be the responsibility of the initiating specialist unless directions have been discussed and agreed with the primary care clinician.
- Termination of treatment will be the responsibility of the specialist.

Initial stabilisation:

Cinacalcet is usually started at a dose of 30mg BD and titrated upwards every two to four months as required – determined by monitoring serum adjusted calcium levels.

The loading period must be prescribed by the initiating specialist.

Maintenance dose (following initial stabilisation):

Will vary patient to patient but this will be the dose required to achieve normocalcaemia (serum adjusted calcium between 2.20 and 2.60mmol/l; usually between 30mg BD and 60mg BD)

The initial maintenance dose must be prescribed by the initiating specialist.

Conditions requiring dose adjustment:

	Serum adjusted calcium	Action to be taken
1.	Adjusted calcium persistently (4 to 6weeks) elevated > 2.60mmol/l	Check compliance Increase cinacalcet dose by 30mg and recheck calcium 4 weeks later. Discuss with consultant endocrinologist if dose greater than 60mg BD required (before increasing).
2.	Adj calcium 2.20 – 2.60mmol/l	Desired level of serum calcium. No dose adjustment required.
3.	Adj Calcium <2.20mmol/l	Stop cinacalcet and repeat blood within two weeks with a view to restarting with lower dose of cinacalcet following discussion with consultant endocrinologist.

6. Pharmaceutical aspects

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Route of administration:	Oral
Formulation:	Tablets
Administration details:	Tablets should not be chewed or crushed. It is recommended that Cinacalcet be taken with food or shortly after a meal.

7. Significant medicine interactions

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The following list is not exhaustive. Please see BNF or SPC for comprehensive information and recommended management.

Medicinal products known to reduce serum calcium.

- Concurrent administration of other medicinal products known to reduce serum calcium and Cinacalcet may result in an increased risk of hypocalcaemia. Patients receiving Cinacalcet should not be given etelcalcetide.

Effect of other medications on cinacalcet

- Cinacalcet is metabolised in part by the enzyme CYP3A4. Co-administration of 200mg ketoconazole BD, a strong inhibitor of CYP3A4, caused an approximate 2-fold increase in cinacalcet levels. Dose adjustment of cinacalcet may be required if a patient receiving cinacalcet initiates or discontinues therapy with a strong inhibitor (e.g., ketoconazole, itraconazole, telithromycin, voriconazole, ritonavir) or inducer (e.g., rifampicin) of this enzyme.
- In vitro data indicate that cinacalcet is in part metabolised by CYP1A2. Smoking induces CYP1A2; the clearance of cinacalcet was observed to be 36-38% higher in smokers than non-smokers. The effect of CYP1A2 inhibitors (e.g. fluvoxamine, ciprofloxacin) on cinacalcet plasma levels has not been studied. Dose adjustment may be necessary if a patient starts or stops smoking or when concomitant treatment with strong CYP1A2 inhibitors is initiated or discontinued.

Effect of cinacalcet on other medications

- Medicinal products metabolised by the enzyme P450 2D6 (CYP2D6): cinacalcet is a strong inhibitor of CYP2D6: Dose adjustments of concomitant medicinal products may be required when cinacalcet is administered with individually titrated, narrow therapeutic index substances that are predominantly metabolised by CYP2D6 (e.g., flecainide, propafenone, metoprolol, desipramine, nortriptyline, clomipramine).

- Desipramine: Concurrent administration of 90 mg cinacalcet once daily with 50 mg desipramine, a tricyclic antidepressant metabolised primarily by CYP2D6, significantly increased desipramine exposure 3.6-fold (90% CI 3.0, 4.4) in CYP2D6 extensive metabolisers.

- Dextromethorphan: Multiple doses of 50 mg cinacalcet increased the AUC of 30 mg dextromethorphan (metabolised primarily by CYP2D6) by 11-fold in CYP2D6 extensive metabolisers.

8. Baseline investigations, initial monitoring and ongoing monitoring to be undertaken by specialist

Monitoring at baseline and during initiation is the responsibility of the specialist; only once the patient is optimised on the chosen medication with no anticipated further changes expected in immediate future will prescribing and monitoring be transferred to primary care.

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		Investigations	Time line
1	Blood tests	Serum bone profile, renal function, serum magnesium, PTH and vita D	Every 6months. (unstable patients may need more frequent monitoring)
2.	Bone DEXA scan	Bone DEXA scan	Every 3 years (or 2 years in osteopenia)
3.	Renal US scan	If symptomatic of renal stone or sudden deterioration of renal function	On initial diagnosis and whenever symptomatic renal stone/CKD

4.	Urinary calcium monitoring	Despite having normal serum calcium, urine calcium could be high, resulting in hypercalciuria and renal stones. This usually resolves following a reduction in serum calcium.	On initial diagnosis and whenever prolonged uncontrolled PHPT
5.	Avoid hypocalcaemia	Particularly in patients with long QT syndrome. Avoid using metoclopramide, gastroprokinetic like domperidone, cisapride and ondansetron if patients have long QT	While taking cinacalcet

When a patient is reviewed, advise primary care whether treatment should be continued, confirm the ongoing dose, and whether the ongoing monitoring outlined in section 9 remains appropriate.

9. Ongoing monitoring requirements to be undertaken by primary care

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See section 10 for further guidance on management of adverse effects/responding to monitoring results.

Monitoring	Frequency
Serum bone profile, renal function, serum magnesium, PTH and vitamin D	Every 6 months (unstable patients may need more frequent monitoring)
Bone DEXA scan (where appropriate; not appropriate in age >84 years)	Every 3 years (every 2 years in osteopenia)
Renal US scan	If symptomatic of renal stone

10. Adverse effects and other management

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Any serious adverse reactions should be reported to the MHRA via the Yellow Card scheme. Visit www.mhra.gov.uk/yellowcard

For information on incidence of ADRs see relevant summaries of product characteristics and for less frequent side effects, see current BNF.

Result	Action for primary care
As well as responding to absolute values in laboratory tests, a rapid change or a consistent trend in any value should prompt caution and extra vigilance	
Hypocalcaemia	See Section 5 regarding Cinacalcet dose titration
QT interval prolongation	Look for drug interactions which prolong QT interval particularly in patients with prolonged QT syndrome. ECG monitoring is only required where symptomatically indicated.
Nausea and Vomiting	Seek advice/guidance from specialist
Upper GI Bleeding	Seek advice/guidance from specialist
Adynamic bone disease. Worsening of bone density decline	Seek advice/guidance from specialist

11. Advice to patients and carers

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The specialist will counsel the patient with regard to the benefits and risks of treatment and will provide the patient with any relevant information and advice, including patient information leaflets on individual medicines.

The patient should be advised to report any of the following signs or symptoms to their primary care prescriber without delay:

- **Symptoms of hypocalcaemia (paraesthesia, myalgia, cramping, tetany, and convulsions)**

The patient should be advised to stop taking cinacalcet and contact their GP.

12. Pregnancy, paternal exposure and breast feeding

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It is the responsibility of the specialist to provide advice on the need for contraception to male and female patients on initiation and at each review, but the ongoing responsibility for providing this advice rests with both the primary care prescriber and the specialist.

Pregnancy:

Contraindicated in pregnancy.

No UKTIS monograph or BUMPs PIL available.

Breastfeeding:

Contraindicated in breastfeeding.

No UKDiLAS monograph available.

13. Specialist contact information

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DBTH Consultant Endocrinologists can be contacted via dbth.diabsec@nhs.net or via telephone on 01302 642608 (DRI) or 01909 572711 (BDGH)

14. Additional information

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Where patient care is transferred from one specialist service or GP practice to another, a new shared care agreement must be completed. Ensure that the specialist is informed in writing of any changes to the patient's GP or their contact details.

15. References

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- British National Formulary (BNF): Cinacalcet via https://www.medicinescomplete.com/#/content/bnf/_615906703
- Primary hyperparathyroidism. NG 132 May 2019 NICE guidelines available via: https://www.nice.org.uk/guidance/ng132
- NHS England Clinical Commissioning Policy for cinacalcet: https://www.england.nhs.uk/wp-content/uploads/2017/06/ccp-cinacalcet-complex-primary-hyperparathyroidism-adults.pdf
- Medical Management of Primary Hyperparathyroidism: Proceedings of the Fourth International Workshop on the Management of Asymptomatic Primary Hyperparathyroidism. J Clin Endocrinol Metab 2014; 99(10):3607–3618
- Cinacalcet normalizes serum calcium in a double-blind randomized, placebo-controlled study in patients with primary hyperparathyroidism with contraindications to surgery: Eur J Endocrinol 2015; 172(5): 527–535. doi:10.1530/EJE-14-0877

16. Other relevant national guidance

- Shared Care for Medicines Guidance – A Standard Approach (RMOC). Available from https://www.sps.nhs.uk/articles/rmoc-shared-care-guidance/
- NHSE policy – Responsibility for prescribing between primary & secondary/tertiary care. Available from https://www.england.nhs.uk/publication/responsibility-for-prescribing-between-primary-and-secondary-tertiary-care/
- General Medical Council. Good practice in prescribing and managing medicines and devices. Shared care. Available from https://www.gmc-uk.org/ethical-guidance/ethical-guidance-for-doctors/good-practice-in-prescribing-and-managing-medicines-and-devices/shared-care
- NICE NG197: Shared decision making. Last updated June 2021. https://www.nice.org.uk/guidance/ng197/.

17. Local arrangements for referral

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Define the referral procedure from hospital to primary care prescriber & route of return should the patient's condition change.

See Section 5 (above).