NHS
Cambridgeshire and Peterborough
Clinical Commissioning Group

Shared Care Guideline

Cinacalcet (Mimpara®) for the management of secondary hyperparathyroidism (SHPT) in patients with chronic renal failure (CRF)

Executive Summary

- For patients with chronic renal failure (CRF), secondary hyperparathyroidism (SHPT) is a condition that develops progressively and is associated with increases in parathyroid hormone levels and derangements in calcium and phosphate metabolism.
- Cinacalcet mimics the action of calcium on the parathytoid cells, suppressing PTH production
- Usual dose of cinacalcet is 30mg-180mg, taken orally, once daily, with food or shortly after a meal
- Patients will be commenced on 30mg once daily. PTH will be monitored two to four weeks post initiation or following dose adjustment and three monthly once established.
- Calcium levels will be monitored weekly for one month following initiation or dose adjustment and one to three monthly thereafter. Phosphate levels will be monitored monthly.
- Cinacalcet is not recommended for the routine treatment of SHPT in patients with end-stage renal disease on **maintenance dialysis therapy. Criteria for use** in the treatment of refractory hyperparathyroidism in patients with end-stage renal disease (including those with calciphylaxis) can be found on page 2.
- The most common adverse effects reported are nausea and vomiting
- Cinacalcet is metabolised in part through cytochrome P450 enzymes CYP3A4 and CYP1A2. Dose adjustment may be required if a patient receiving cinacalcet initiates or discontinues therapy with a strong inhibitor or inducer of CYP3A4
- Cinacalcet should not be used whilst breast-feeding. It should only be used in pregnancy if the potential benefit justifies the potential risk to the foetus.
- The responsibilities of the hospital specialist, GP and patient for this Shared Care Guideline can be found in section 11.

Sharing of care depends on communication between the specialist, GP and the patient or their parent/carer. The intention to share care should be explained to the patient and accepted by them. Patients are under regular follow-up and this provides an opportunity to discuss drug therapy. The doctor/healthcare professional who prescribes the medication has the clinical responsibility for the drug and the consequences of its use. Further information about the general responsibilities of the hospital specialist and GP can be found here

1. Scope

Prescribing by General Practitioners

2. Aim

Cinacalcet is used to manage hyperparathyroidism in patients with chronic renal failure. This shared care guideline outlines the responsibilities of primary and secondary care clinicians using cinacalcet for SHPT in patients with chronic renal failure.

3. Introduction

For patients with chronic kidney disease (CKD), secondary hyperparathyroidism (SHPT) is a condition that develops progressively and is associated with increases in parathyroid hormone (PTH) levels and derangements in calcium and phosphate metabolism. The goals of treatment of SHPT are to lower levels of PTH, Calcium and phosphate in the blood, to prevent progressive bone disease and the systemic consequences of disordered mineral metabolism.

Cinacalcet is the first in a new class of calcimimetic agents, used to treat SHPT in CKD patients. It 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 not recommended for the routine treatment of SHPT in patients with end-stage renal disease on maintenance dialysis therapy.

Cinacalcet is recommended for the treatment of refractory hyperparathyroidism in patients with end-stage renal disease (including those with calciphylaxis) **only in those:**

a) Who have very uncontrolled plasma levels of intact parathyroid hormone (defined as greater than 85 pmol/l (800pg/ml) that are refractory to standard therapy, and a normal or high adjusted serum calcium level, **and**

b) In whom surgical parathyroidectomy is contraindicated, in that the risks of surgery are considered to outweigh the benefits.

c) 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 four months of treatment, including dose escalation as appropriate.

Clinical studies have consistently demonstrated that elevated PTH, Calcium and phosphate due to SHPT are associated with increased morbidity and mortality, with clinical manifestations of SHPT such as soft tissue and vascular calcification, and cardiovascular complications including death. Cinacalcet has also been shown to reduce the incidence of fractures and the need for parathyroidectomy.

4. Abbreviations

- SHPT: Secondary hyperparathyroidism
- CRF: Chronic Renal Failure
- GP: General Practitioner
- PTH: Parathyroid Hormone
- GI: Gastrointestinal
- CSM: Committee for the safety of medicines
- iPTH: intact parathyroid hormone
- CYP (e.g. CYP3A4): cytochrome P450 enzyme (specific enzyme)
- CKD: Chronic Kidney Disease

5. Dose and Administration

- Usual dose of cinacalcet is 30mg-180mg, taken orally, once daily
- Cinacalcet should be swallowed whole, with food or shortly after a meal as this increases bioavailability.
- The dose can be titrated every two to four weeks to a maximum dose of 180mg, aiming to achieve a target PTH level of 150-300pg/ml.

Further information can be found in the Summary of Product Characteristics
https://www.medicines.org.uk/emc/product/5599

6. Adverse Effects

In controlled studies the most common adverse effect reported were GI disturbance with nausea and vomiting, in most cases this was mild to moderate in severity and transient in nature.

Another significant problem is hypocalcaemia which has been linked to an increased risk of seizure and paraesthesia in cinacalcet treated patients.

A lowering of testosterone levels has also been reported.

Very common (≥ 1 in 10)
Nausea and Vomiting

Common (≥ 1 in 100 and < 1 in 10)
Hypersensitivity reactions (angioedema and urticaria)
Rash
Anorexia
Dizziness
Dyspepsia
Myalgia
Asthenia

All serious adverse events should be reported to the CSM through the Yellow Card reporting scheme.

Further information can be found in the Summary of Product Characteristics
https://www.medicines.org.uk/emc/product/5599

7. Cautions

- Cinacalcet treatment should not be initiated in patients with serum calcium (corrected for albumin) below the lower limit of the normal range. Since cinacalcet lowers serum calcium, patients should be monitored carefully for the occurrence of hypocalcaemia.
- A dynamic bone disease may develop if PTH levels are chronically suppressed below approximately 1.5 times the upper limit of normal with the iPTH assay. If PTH levels decrease below the recommended target range in patients treated with Cinacalcet, the dose of Cinacalcet and/or vitamin D sterols should be reduced or therapy discontinued.
- The threshold for seizures is lowered by significant reductions in serum calcium levels.

Further information can be found in the Summary of Product Characteristics
https://www.medicines.org.uk/emc/product/5599

8. Contraindications

- Hypersensitivity to the active substance or any of the excipients.
- Safety and efficacy have not been established in patients below the age of 18 years.
- Cinacalcet should only be used in pregnancy if the potential benefit justifies the potential risk to the foetus. It should not be used whilst breast-feeding.

Further information can be found in the Summary of Product Characteristics
https://www.medicines.org.uk/emc/product/5599

9. Interactions

- Cinacalcet is metabolised in part through cytochrome P450 enzymes CYP3A4 and CYP1A2.
- Dose adjustment may be required if a patient receiving cinacalcet initiates or discontinues therapy with a strong inhibitor (eg azoles, telithromycin, ritanovir) or inducer (eg rifampicin) of CYP3A4.
- Smoking induces CYP1A2 and clearance of cinacalcet is higher in smokers than non-smokers. The effect of CYP1A2 inhibitors (eg fluvoxamine, ciprofloxacin) is not known but may impact on dosage if these drugs are discontinued or initiated.

Further information can be found in the Summary of Product Characteristics
https://www.medicines.org.uk/emc/product/5599

Monitoring Standards & Actions to take in the event of abnormal test results/symptoms

Patients will be commenced on 30mg once daily. PTH will be monitored two to four weeks post initiation or following dose adjustment and three monthly once established.

Calcium levels will be monitored weekly for one month following initiation or dose adjustment and one to three monthly thereafter. Phosphate levels will be monitored monthly. **All monitoring will be performed by the hospital specialist**.

10. Shared Care Responsibilities

a. Hospital specialist:

- Send a letter to the GP requesting shared care for the patient.
- Inform the GP after each clinic attendance if there is any change to treatment or monitoring.
- Inform GP of patients who do not attend clinic appointments.
- To provide any advice to the patient/carer when requested.
- Advise GP on review, duration or discontinuation of treatment where necessary.
- Monitor smoking status of patient and review dosing if this changes (smoking reduces plasma levels of Cinacalcet). Explain the effect of smoking on therapy and encourage smokers to quit.
- Evaluate any reported adverse effects by GP or patient

b. General Practitioner:

- Agreement to shared care guideline by the GP.
- Prescribe the drug treatment as described
- Report any adverse events to the hospital specialist, where appropriate.
- Request advice from the hospital specialist when necessary.
- Inform hospital specialist if any new medication that may interfere with cinacalcet is commenced
- Monitor smoking status of patient and seek guidance from specialist if this changes (smoking reduces plasma levels of Cinacalcet). Explain the effect of smoking on therapy and encourage smokers to quit, supporting the consultant/ specialist nurse in achieving this.

c. Patient or parent/carer:

- Report to the hospital specialist or GP if they do not have a clear understanding of their treatment.
- Patients must not exceed the recommended dose.
- Patients must attend their scheduled clinic and blood test appointments (where relevant).
- Must inform other clinical staff that they are receiving treatment.
- Report any adverse effects to the hospital specialist or GP.
- Attempt to cease smoking and notify any change in smoking status to GP/ specialist.

11. Contact numbers for advice and support

North West Anglia NHS Foundation Trust		
Specialist	**Post**	**Telephone**
Dr Frieder Kleeman	Consultant Nephrologist	01733 673699
Dr Bahareh Arsalanizadeh	Consultant Nephrologist	01733 673699
Dr Asmaa Al-chidadi	Consultant Nephrologist	01733 673699
Dr Soubhik Pal	Consultant Nephrologist	01733 673699
Dr Sourjya Kar	Consultant Nephrologist	01733 673699

12. Equality and Diversity Statement

This document complies with the Cambridge University Hospitals NHS Trust service Equality and Diversity statement.

13. Disclaimer

It is your responsibility to check that this printed out copy is the most recent issue of this document.

14. Document Management

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The information contained in this guideline is issued on the understanding that it is accurate based on the resources at the time of issue. For further information please refer to the most recent Summary of Product Characteristics https://www.medicines.org.uk/emc/product/5599