HERPC

Hull & East Riding Prescribing Committee

Prescribing Framework for Cinacalcet for the treatment of secondary hyperparathyroidism in patients with end stage renal disease

Patient's Name:…….… NHS Number: ……

Patient's Address:……..……(Use addressograph sticker)

GP's Name:……..

Communication

We agree to treat this patient within this Prescribing Framework

Specialist Prescriber's Name…… Prof Reg. No. ……

Specialist Prescriber's Signature…… Date:……

Where prescriber is <u>not</u> a consultant:

Consultant's Name: …… GMC No ……..

Consultant's Signature ……..... ……. Date:…….

GP's Signature:…… Date:……..

GP's Name (if different from listed above)……..

The front page of this form should be completed by the specialist and the form sent to the patient's general practitioner.

The patient's GP should sign and **send back to specialist**, to confirm agreement to enter into shared care arrangement. If the General Practitioner is **<u>unwilling</u>** to accept prescribing responsibility for the above patient the specialist should be informed within two weeks of receipt of this framework and specialist's letter.

Full copy of framework can also be found at:
https://www.hey.nhs.uk/herpc/amber/

1. Background

These guidelines aim to provide a framework for the prescribing of cinacalcet by GPs and to set out the associated responsibilities of GPs and hospital specialists who enter into the shared care arrangements.

Secondary hyperparathyroidism occurs in patients with chronic kidney disease, where increasing serum phosphate and decreasing active vitamin D result in a reduction in serum calcium. Parathyroid hormone (PTH) production is increased to compensate. Due to renal failure, active vitamin D levels remain low and PTH levels continue to rise. PTH causes phosphate and calcium to be released from bone. Over a prolonged period this leads to renal osteodystrophy, bone pain and fracture, soft tissue and vascular calcification and cardiovascular complications. If the Calcium x phosphate product (obtained by multiplying serum phosphate and calcium level) and PTH are raised this has been shown to be a poor prognostic marker.

Current treatment options for Secondary hyperparathyroidism include

- Dietary inorganic phosphate restriction
- Phosphate binders (calcium carbonate, calcium acetate, sevelamer, sucroferric oxyhydroxide, lanthanum carbonate
- 1-alfacalcidol
- Parathyroidectomy

Following the NICE review (TAG117) it was recommended that cinacalcet may be used for refractory secondary hyperparathyroidism in patients with end stage renal disease on maintenance dialysis and:

- "very uncontrolled" plasma PTH >84pmol/L (>800pg/mL)) that is refractory to standard treatment

AND

- in whom surgical parathyroidectomy is contraindicated (i.e. risk of surgery is greater than potential benefit)

In addition NICE stated that treatment should be monitored regularly and only continued if a reduction in PTH of greater than 30% is seen within 4 months of treatment.

This document should be read in conjunction with the guidance "Responsibility for prescribing between Primary & Secondary/Tertiary Care" https://www.england.nhs.uk/wp-content/uploads/2018/03/responsibility-prescribing-between-primary-secondary-care-v2.pdf

2. Indication

Secondary hyperparathyroidism in patients on maintenance dialysis who have PTH >84pmol/L (>800pg/mL) despite standard therapy and would not be amenable to surgical intervention.

The first 4 months will be supplied by the specialist. After 4 months response to treatment will be assessed, if PTH has fallen by 30% or more then the GP will be asked to continue treatment.

3. Dose

Starting dose is 30mg once a day. **It is vital that doses are titrated to achieve a response; doses may be adjusted every** 2 to 4 weeks to achieve a target PTH of 15.9 - 31.8pmol/L (150 – 300pg/mL). Maximum dose is 180mg once a day. The dose should be taken with or shortly after food. Patients who demonstrate a sub-optimal response to treatment should have their dose reviewed; this will be done by the specialist.

4. Duration of treatment

Initial treatment will be for 4 months. After the initial phase patient's response to treatment will be assessed. If the PTH levels have been reduced by at least 30% then treatment will continue. In patients who have responded it is likely that treatment will continue long term.

5. Contraindications and cautions

Cinacalcet should not be initiated in

- patients with serum calcium below lower limit of normal range (corrected for albumin).
- CKD patients who are NOT on dialysis (increased risk of hypocalcaemia)

Cautions

- Hypocalcaemia
- Hepatic impairment – close monitoring and dose adjustment may be required
- Patients with seizures – the seizure threshold is lowered by significant reductions in serum calcium levels
- Hypotension – idiosyncratic cases of hypotension have been reported in patients with impaired cardiac function
- Heart failure – idiosyncratic cases of worsening heart failure have been reported in patients with impaired cardiac function
- Pregnancy - There are no clinical data from the use of cinacalcet in pregnant women It should be used during pregnancy only if the potential benefit justifies the potential risk to the foetus. Any planned or unplanned pregnancy should be discussed with the specialist.
- Breast feeding - It is not known whether cinacalcet is excreted in human milk and patients should therefore be advised not to breast feed.

6. Adverse effects

Gastrointestinal side effects - nausea and vomiting commonly reported but generally mild/moderate in nature and usually transient. Anorexia is also commonly reported. Less commonly diarrhoea and dyspepsia
Central nervous system - commonly dizziness, paraesthesia and seizures (see above under warnings)
Cardiac – isolated reports of hypotension and/ or worsening heart failure in patients with impaired cardiac function. Also isolated reports of QT prolongation and ventricular arrhythmia secondary to hypocalcaemia.
Allergic reactions – hypersensitivity reactions are uncommon
Rashes – common
Asthenia – common
Hypocalcaemia – a reduction in serum calcium is part of the pharmacological effect of cinacalcet, however, symptomatic hypocalcaemia may occur and be responsible for isolated reports of arrhythmias, seizures.
More common symptoms would be paraesthesia, myalgia, cramping. In the event of hypocalcaemia the specialist may advise prescription of calcium containing phosphate binders and alfacalcidol.
Adjustment of dialysis fluid calcium concentrations can be used to raise serum calcium.

7. Interactions

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.

Smoking – increases clearance of cinacalcet as it induces the CYP1A2 enzyme. Dose adjustment of cinacalcet may be required if a patient starts or stops smoking.

Details of contraindications, cautions, drug interactions and adverse effects listed above are not exhaustive. For further information always check with BNF www.bnf.org.uk or SPC (www.medicines.org.uk).

8. Monitoring

Patients receiving cinacalcet will be on maintenance dialysis, therefore all biochemical parameters will be monitored by the renal unit. Monitoring is as follows (consultants may choose different monitoring regimens).

Initiation phase:
Calcium and phosphate weekly
PTH monitor monthly

Maintenance phase:
Calcium and Phosphate monthly
PTH every 3 months

In addition to the above monitoring Calcium and phosphate should be checked within a week of dose adjustments.

9. Information to patient

Patients will be advised of benefits and risks of treatment, including adverse reactions listed on Section 6.

10. Responsibilities of clinicians involved

Stage of Treatment	Hospital Specialist	General Practitioner
Initiation	-Diagnose and select appropriate patients for treatment. -Initiate and provide treatment with cinacalcet for the first 4 months of treatment. -Inform GP that patient has commenced treatment -Inform GP of response after 4months and if treatment is to continue, ask GP to prescribe. -Send prescribing framework to GP	-Respond to specialist informing if willing to continue treatment past 4 month.
Monitoring	Check PTH, Serum calcium and phosphate as detailed in section 8. Inform GP of relevant results Advise GP on dose adjustments in an effort to achieve 30% reduction in PTH Stop treatment if no response is demonstrated after 4 months.	Monitor patient for adverse effects and inform specialist where relevant. Adjust dose when requested by specialist

Contact Details:

During Office hours:

- Renal consultant may be contacted via the hospital switchboard (01482 875875) or see clinic letter.
- Specialist Renal Pharmacist, tel. 01482 674043

Out of hours:
The on call renal specialty trainee or consultant may be contacted via the hospital switchboard (01482 875875).

APPROVAL PROCESS

Written by:	***Paul Kendrew, Renal Pharmacist, HEY***
Consultation process:	***Renal specialist team***
Approved by:	***MMIG November 2012***
Ratified by:	***HERPC November 2012 Updated June 2018 Updated September 2021***
Review date:	***September 2024***