Shared Care Guideline for Cinacalcet for Primary Hyperparathyroidism in Adults (GP Summary)

It is essential that a transfer of care only takes place with agreement of the GP and when sufficient information has been received. If the GP does not agree to share care they will inform the Consultant responsible for the patient's care.

Basingstoke, Southampton & Winchester District Prescribing Committee

Specialist Contact Details	**Patient ID Label**
Name: _____	**Surname:** _____
Location: _____	**Forename:** _____
Date: _____	**NHS Number:** _____
Tel: _____	**Date of Birth:** _____

Indications	Primary hyperparathyroidism is a common disorder characterised by chronically elevated levels of serum calcium and parathyroid hormone. Patients with moderate to severe disease may develop nephrolithiasis, osteoporosis or symptoms of hypercalcaemia including neuromuscular weakness, fatigue and impaired cognitive function. Parathyroidectomy is the primary treatment and is curative in 95% of cases. Cinacalcet is indicated for the treatment of significant hypercalcaemia (corrected calcium>3.0mmol/l) or symptomatic hypercalcaemia (corrected calcium)>2.85mmol/l due to primary hyperparathyroidism where parathyroidectomy is contraindicated, unsuccessful or not clinically appropriate.
Dose & response	**The starting dose of cinacalcet is 30mg twice daily**. The calcium lowering effect is present within two to three weeks (85-90%). Serum corrected calcium should be checked one week after initiation and the dose may be titrated every 2 to 4 weeks according to response to a **maximum dose of 90mg four times daily**.
Specialist responsibilities	**Roles to be undertaken by initiating endocrinologist or specialist** 1. Initiate treatment and titrate until a maintenance dose is achieved. 2. Undertake baseline monitoring and blood tests during initial titration. 3. Monitor patient's initial reaction to and progress on the drug. 4. Ensure that the patient has an adequate supply of medication until GP supply can be arranged. 5. Provide GP with advice on when to stop this drug. 6. Advise on cinacalcet dose adjustments when contacted by the GP in accordance with this guideline 7. Provide patient with relevant drug information to enable understanding of potential side effects and appropriate action 8. Provide patient with relevant drug information to enable understanding of the role of monitoring.
GP Responsibilities	**Key roles to be undertaken in primary care once a decision to work under shared care is made** 1. To continue to prescribe cinacalcet as specified by the initiating specialist in line with this shared care guideline 2. Monitor the smoking status of the patient (Clearance of cinacalcet is higher in smokers than non-smokers) inform and seek advice and guidance from the specialist if this changes significantly. 3. Ensure no drug interactions with concomitant or newly prescribed medicines. 4. Monitor and prescribe in collaboration with the specialist according to this protocol. 5. Ensure symptoms or results are appropriately actioned, recorded and communicated to secondary care when necessary. 6. Stop treatment on the advice of the specialist or immediately if an urgent need to stop treatment arises. 7. Ensure the monitoring and dosage record is kept up to date 8. Report adverse event s to the MHRA on a Yellow Card www.mhra.gov.uk/yellowcard and to the specialist.
Primary care monitoring	Initial diagnostic and monitoring blood tests will be undertaken by the specialist to establish a stable dose regime (unless specifically agreed with the GP). Primary care to monitor

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Serum corrected calcium and phosphate 1 week after any dose adjustment or following initiation/discontinuation of any interacting medication or change in smoking status.
Serum corrected calcium every 3 months, once maintenance dose levels have been established

The aim of the treatment is to maintain adjusted calcium (corrected calcium) between 2.20 and 2.60 mmol/l as per monitoring table below.
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<tr><td>Actions to be taken in response to monitoring</td><td>
If clinically relevant reductions in serum calcium are not maintained, consider discontinuation of cinacalcet therapy with specialist input.

If calcium levels become abnormal during treatment, the endocrinologist should be notified in each case. If marginally out of range repeat test before action.

<table>
<tr><th>Corrected Calcium Level</th><th>Action for GPs</th></tr>
<tr><td>>2.60</td><td>Check compliance. Seek specialist advice as patient will require dose increase.</td></tr>
<tr><td>2.20 – 2.60</td><td>Dose review – If tolerated no further action required</td></tr>
<tr><td><2.20</td><td>Stop cinacalcet. Recheck calcium after one week. Seek specialist advice, likely resume at significantly lower dose.</td></tr>
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<tr><td>Contra-indications</td><td>
Cinacalcet is contraindicated in:

Known hypersensitivity to the drug or any of its excipients
Hypocalcaemia
Pregnancy/breastfeeding
Hereditary problems with galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption.

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<tr><td>Cautions (please note this does not replace the SPC or BNF and should be read in conjunction with it).</td><td>
Use with caution in patients with:

Epilepsy – seizures may occur in hypocalcaemia and significant reductions in serum calcium can lower seizure threshold, therefore close monitoring (monthly until calcium stabilised) is advised in those with a seizures disorder.
Hepatic impairment – Cinacalcet can accumulate in patients with moderate to severe hepatic impairment (Child-Pugh B, C). Plasma levels could rise by 2-3 fold, therefore treatment in these patients should be closely monitored for signs and symptoms of hypocalcaemia, consider checking their PTH, Serum corrected calcium and phosphate if suspect hypocalcaemia. In case of discontinuation or dose adjustment then please check again in 1 week (please see primary care monitoring).
Heart failure/prolonged QT interval – isolated cases of hypotension and/or worsening heart failure have been reported in patients with impaired cardiac function.
Pregnancy - Cinacalcet may be used on specialist advice where benefit outweighs potential harm to foetus
Breastfeeding – it is not known whether cinacalcet is excreted in breast milk. A decision should be made to discontinue either breastfeeding or treatment with cinacalcet.

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<tr><td>Important adverse effects & management</td><td>
Specialist to detail below the action to be taken upon occurrence of a particular adverse event as appropriate. Most serious toxicity is seen with long-term use and may therefore present first to GPs.

<table>
<tr><th>Adverse Event</th><th>Action to be taken</th><th>By whom</th></tr>
<tr><td>Hypocalcaemia – any signs of: paraesthesias, myalgias, cramping, tetany, prolonged QT, arrhythmia and convulsions (common)</td><td>Stop drug.</td><td>GP/Specialist</td></tr>
<tr><td>Worsening Liver Function</td><td>Stop drug.</td><td>GP/Specialist</td></tr>
<tr><td>Seizures - may be secondary to hypocalcaemia leading to reduced seizure threshold</td><td>Stop drug</td><td>GP/specialist</td></tr>
<tr><td>Nausea and Vomiting - normally transient (common)</td><td>Provide symptomatic relief. If symptoms persistent then refer back to specialist.</td><td>GP</td></tr>
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	Dyspepsia, decreased appetite, anorexia (common)	Provide symptomatic relief. If symptoms persistent then refer back to specialist.	GP
	Constipation or diarrhoea (common)	Provide symptomatic relief. If symptoms persistent then refer back to specialist.	GP
	Hypersensitivity, rash (common)	Stop drug	GP/Specialist
	Dizziness, headaches (common)	Provide symptomatic relief. If symptoms persistent then refer back to specialist.	GP
	Chest infection, cough, dyspnoea (common)	Provide symptomatic relief. If symptoms persistent then refer back to specialist.	GP
	Asthenia (common)	If persistent consult specialist.	GP
	Hyperkalaemia (common)	Treat. If severe and persistent refer back to specialist.	GP
	Reduced testosterone levels (common)	Consult specialist for advice.	GP

Important Drug Interactions (consult the Summary of Product Characteristics or BNF for a comprehensive list)	**The following drugs must not be prescribed without consultation with the specialist.** **CYP3A4** Cinacalcet is a substrate of the liver enzyme CYP3A4. Hence any inhibition or induction of this enzyme will affect the levels of cinacalcet. **CYP3A4 inhibitors:** The following are CYP3A4 inhibitors which can increase the half-life of cinacalcet, leading to accumulation. On initiation or termination of these inhibitors, dose adjustment of cinacalcet is required. • Antifungals: Ketoconazole, Itraconazole, Voriconazole • Telithromycin • Ritonavir **CYP3A4 inducers:** These will reduce the half-life of cinacalcet eg: rifampicin **CYP2D6** Cinacalcet is a potent inhibitor of CYP2D6 enzyme; hence any metabolism that involves CYP2D6 substrates would be reduced. Leading to an increase of these substrates:- • Tricyclic antidepressants • Flecainide • Metoprolol • Tamoxifen - cinacalcet may inhibit the metabolism of tamoxifen to its active form. Therefore reducing the efficacy of tamoxifen. The following drugs may be prescribed with caution: **CYP1A2** CYP1A2 metabolises cinacalcet **CYP1A2 inhibitors:** The following increase the half-life of cinacalcet by inhibiting CYP1A2 enzymes e.g. • Ciprofloxacin • Fluvoxamine **CYP1A2 inducers:** These reduce the half-life of cinacalcet e.g. Smoking: close monitoring of the patient's smoking status is required. Dose adjustments of cinacalcet may be required if smoking status changes during treatment. **Warfarin is not affected by cinacalcet.**

The manufacturer's summary of product characteristics (SPC) and the most current edition of the British National Formulary should be consulted for full information on contraindications, warnings, side effects and drug interactions.

References

1. Summary of product characteristics for Cinacalcet (Mimpara) Amgen Ltd. Date accessed December 20
2. British National Formulary January 2020.
3. NHS England Clinical Commissioning Policy: Cinacalcet for Complex Primary Hyperparathyroidism in Adults