The Pennine Acute Hospitals NHS
NHS Trust

NHS

Greater Manchester Interface Prescribing Group Shared Care Template

Shared Care Guideline for *Cinacalcet primary hyperparathyroidism*		**Reference Number**
Author(s)/Originator(s): (please state author name and department) *P K Prakash, Consultant Physician / Endocrinologist, Pennine Acute Trust*		**To be read in conjunction with the following documents:** Current Summary of Product characteristics (http://www.medicines.org.uk) BNF
Date approved by Commissioners: *13/06/2014*	**Review Date:** *13/06/2017*	

Please complete all sections

1. Licensed Indications	Treatment of primary hyperparathyroidism when parathyroid surgery (parathyroidectomy) is clinically inappropriate (when corrected calcium levels are greater than 3.0 mmol/L).
2. Therapeutic use & background	Primary hyperparathyroidism is a common disorder that is often diagnosed as a result of biochemical screening or as part of evaluation of decreased bone mass. It is normally seen with hypercalcaemia. Patients with symptomatic primary hyperparathyroidism should have surgery as parathyroidectomy is the only cure. This Shared Care guideline applies to patients with primary hyperparathyroidism who are unsuitable/ unfit for surgery. Cinacalcet is a calcimimetic that increases the sensitivity of the calcium sensing receptor on the parathyroid to extracellular calcium, thereby inhibiting parathyroid hormone (PTH) secretion. The inhibition of PTH secretion then leads to a reduction in calcium levels.

3. Contraindications (please note this does not replace the SPC or BNF and should be read in conjunction with it).	• Known hypersensitivity to the drug
	• Pregnancy / breast-feeding
	• Less than 18 years old
	• Hypocalcaemia
	• Hereditary problems of galactose intolerance- Lapp lactase deficiency or glucose-galactose malabsorption.
	• Use with caution in patients with :
	  o Epilepsy
	  o Moderate to severe hepatic insufficiency (Child-Pugh: Class B, C):-. As reduced hepatic function can increase the half life of cinacalcet hence leading to accumulation of cinacalcet. Close monitoring is advised.
	  o Heart failure- In post-marketing safety surveillance, isolated, idiosyncratic cases of hypotension and/ or worsening heart failure have been reported in patients with impaired cardiac function.

4. Prescribing in pregnancy and	*Pregnancy*: Use within this group is not recommended unless it is under specialist advice- There is no data available for the use of cinacalcet within pregnant women. Although no

<table>
<tr><td>lactation</td><td>direct harmful effects have been seen in pregnancy, parturition or postnatal development, use during pregnancy is not warranted unless the benefits outweigh the potential risks to the foetus.

Lactation: Use within this group is not recommended unless it is under specialist advice-. There have been no data to show the abundance of cinacalcet within human milk.</td></tr>
<tr><td rowspan="8">5. Dosage regimen for continuing care</td><td>Route of administration | Oral</td></tr>
<tr><td>Preparations available (include in this section any necessary information relating to availability of special preparations for children or those with swallowing difficulties)

Cinacalcet tablets: 30 mg, 60 mg and 90 mg</td></tr>
<tr><td>Insert dose to be prescribed including units, frequency and duration of treatment.
Please prescribe: 30 mg –90mg twice daily (max up to 90mg QDS)</td></tr>
<tr><td>Is titration required | Yes (complete the following section)</td></tr>
<tr><td>The recommended starting dose of cinacalcet for adults is 30 mg twice per day. The dose of cinacalcet should be titrated every 2 to 4 weeks through sequential doses of 30 mg twice daily, 60 mg twice daily, 90 mg twice daily, and 90 mg three or four times daily as necessary to reduce serum calcium concentration to or below the upper limit of normal. The maximum dose used in clinical trials was 90 mg four times daily.</td></tr>
<tr><td>Adjunctive treatment regime
Adequate hydration</td></tr>
<tr><td>Conditions requiring dose reduction
e.g. impaired renal/ liver function
Caution in patients with moderate to severe hepatic impairment – No specific dose reducing regimen. Please monitor patient for signs of hypocalcaemia closely and stop in the event of hypocalcaemia. As hepatic impairment can induce accumulation of cinacalcet by 2 -3 folds. See section 3</td></tr>
<tr><td>Usual response time

Two to four weeks</td></tr>
<tr><td>Duration of treatment

Long-term / specified by Endocrinologist</td></tr>
<tr><td>Treatment to be terminated by Consultant Endocrinologist, GP after discussion with patient.</td></tr>
<tr><td>NB. All dose adjustments will be the responsibility of the initiating specialist care unless directions have been specified in the medical letter to the GP.</td></tr>
<tr><td>6.Drug Interactions For a comprehensive</td><td>The following drugs must not be prescribed without consultation with the specialist:</td></tr>
</table>

list consult the BNF or Summary of Product Characteristics	**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 cause a two fold increase in cinacalcet levels. This will result in an increased cinacalcet half-life, ultimately leading to cinacalcet accumulation. On termination or initiation of these inhibitors, dose adjustment of cinacalcet is required. • Ketoconazole. • Itraconazole • Telithromycin • Voriconazole • 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 • 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 by inducing CYP1A2 enzymes e.g. Smoking- close monitoring of the patient's smoking status is required and adequate adjustments of cinacalcet carried out. Cinacalcet does not have an interaction with warfarin
7. Adverse drug reactions *For a comprehensive list*	**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.**

(including rare and very rare adverse effects), or if significance of possible adverse event uncertain, consult Summary of Product Characteristics or BNF	**Adverse event** System – symptom/sign	**Action to be taken** Include whether drug should be stopped prior to contacting secondary care specialist	**By whom**
	Hypocalcaemia- Any signs of: paraesthesias, myalgias, cramping, tetany, prolonged QT, *arrhythmia* and convulsions *(common)*	*Stop drug*	*GP or consultant*
	Worsening liver function	*Stop drug*	*GP or consultant*
	Seizures- this may be secondary to hypocalcaemia leading to a reduction of seizure threshold	*Stop drug*	*GP or consultant*
	Nausea and vomiting – *normally transient (common)*	*Provide symptomatic relief. If symptoms persistent refer back to the specialist*	*Gp*
	Dyspepsia, decreased appetite, anorexia *(common)*	*Provide symptomatic relief. If symptoms persistent refer back to the specialist*	*GP*
	Constipation or diarrhoea *(common)*	*Provide symptomatic relief. If symptoms persistent refer back to the specialist*	*GP*
	Hypersensitivity, rash *(common)*	*Stop*	*GP/ consultant*
	Dizziness, headaches *(common)*	*Provide symptomatic relief. If symptoms persistent refer back to the specialist*	*GP*
	Worsening heart failure, hypotension (unknown)	*Provide symptomatic relief. If symptoms persistent refer back to the specialist*	*GP*
	Chest infection, cough, dyspnoea *(common)*	*Provide symptomatic relief. If symptoms persistent refer back to the specialist*	*GP*
	Asthenia *(common)*	*If persistent – consult specialist*	*GP*
	Hyperkalaemia *(common)*	*Treat. If severe and persistent then refer back to the specialist*	*GP*

	Reduced testosterone levels *(common)*	*Consult specialist for advice*	*GP*
	The patient should be advised to report any of the following signs or symptoms to their GP without delay: Signs of hypocalcaemia - paraesthesias, myalgias, cramping, tetany and convulsions		
	Other important co-morbidities (e.g. Chickenpox exposure). Include advice on management and prevention and who will be responsible for this in each case:		
	Any adverse reaction to a black triangle drug or serious reaction to an established drug should be reported to the MHRA via the "Yellow Card" scheme.		
8.Baseline investigations	***List of investigations / monitoring undertaken by secondary care*** Baseline tests carried out within secondary care: Calcium before start, 2 weeks after initiation of drug Parathyroid hormone (PTH) Urea Electrolytes Creatinine Liver function tests (LFT) Phosphates Smoking status		
9. Ongoing monitoring requirements to be undertaken by GP	**Is monitoring required?**	**Yes or No (if yes complete following section)** Yes	

Monitoring	**Frequency**	**Results**	**Action**	**By whom**
Calcium (total serum)	2-3 monthly	*2.2- 2.6*	*Dose review*	*GP*
		<2.2	*Stop the medication and refer back to the Endocrinologist.*	*GP*
		>2.6	*Refer back to the Endocrinologist for dose review.*	*GP*
Smoking status		*Stopped or started Smoking?*	*If smoking status altered then GP to inform Endocrinologist. Endocrinologist will review dose*	*GP*

10. Pharmaceutical aspects	*e.g. special storage requirements, washout periods Or where there are "no special considerations"* *Cinacalcet should be taken with food or after food as studies have shown that this increases the bioavailability of the medication*
11. Secondary care contact information	**If stopping medication or needing advice please contact:**
	Dr *[insert text here]*_____
	Contact number: *[insert text here]*_____
	Hospital: *[insert text here]*_____
12. Criteria for shared care	Prescribing responsibility will only be transferred when ▪ Treatment is for a specified indication and duration. ▪ Treatment has been initiated and maintenance dose achieved by the secondary care specialist. ▪ The patient's initial reaction to and progress on the drug is satisfactory. ▪ The GP has agreed in writing in each individual case that shared care is appropriate. ▪ The patient's general physical, mental and social circumstances are such that he/she would benefit from shared care arrangements

13. Responsibilities of initiating specialist	Initiate treatment and titrate until a stable maintenance dose is achieved. Undertake baseline monitoring. Dose adjustments. Monitor patient's initial reaction to and progress on the drug. Ensure that the patient has an adequate supply of medication until GP supply can be arranged. Continue to monitor and supervise the patient according to this protocol, while the patient remains on this drug, and agree to review the patient promptly if contacted by the GP Provide GP with diagnosis, relevant clinical information and baseline results, treatment to date and treatment plan, duration of treatment before consultant review. Provide GP with details of outpatient consultations, ideally within 14 days of seeing the patient *or* inform GP if the patient does not attend appointment Provide GP with advice on when to stop this drug. Provide patient with relevant drug information to enable Informed consent to therapy Provide patient with relevant drug information to enable understanding of potential side effects and appropriate action Provide patient with relevant drug information to enable understanding of the role of monitoring.
14. Responsibilities of the GP	---------- Continue treatment once maintenance dose has been achieved by the specialist. Ensure no drug interactions with concomitant medicines To monitor and prescribe in collaboration with the specialist according to this protocol To ensure that the monitoring and dosage record is kept up to date To undertake vaccination as directed by the initiating consultant, the BNF or Green Book Symptoms or results are appropriately actioned, recorded and communicated to secondary care when necessary.
15. Responsibilities of the patient	---------- To take medication as directed by the prescriber, or to contact the GP if not taking medication Failure to attend will result in medication being stopped (on specialist advice). To report adverse effects to their Specialist or GP.

16.Additional Responsibilities	**List any special considerations**	**Action required**	**By whom**	**Date**
				[insert]
	[insert]	***[insert]***	***[insert]***	***[insert]***
17. Supporting documentation	The SCG must be accompanied by a patient information leaflet.			
18. Shared care agreement form	Attached below			

Shared Care Agreement Form

Specialist request

***IMPORTANT: ACTION NEEDED**

Dear Dr *[insert Doctors name here]*

Patient name: *[insert Patients name here]*
Date of birth: *[insert date of birth]*
Diagnosis: *[insert diagnosis here]*

This patient is suitable for treatment with cinacalcet for the treatment of *primary hyperparathyroidism*.

This drug has been accepted for Shared Care according to the enclosed protocol (as agreed by Trust / LHB / AWMSG). I am therefore requesting your agreement to share the care of this patient.

Treatment was started on *[insert date started]* *[insert dose and frequency].*

If you are in agreement, please undertake monitoring and treatment from *[insert date]*
NB: date must be at least 1 month from initiation of treatment.

Baseline tests: serum corrected calcium, smoking status.

Next review with this department: *[insert date]*
You will be sent a written summary within 14 days. The medical staff of the department are available at all times to give you advice. The patient will not be discharged from out-patient follow-up while taking *[insert text here]*.

Please use the reply slip overleaf and return it as soon as possible.

Thank you.

Yours

[insert Specialist name]

Shared Care Agreement Form

GP Response

Dear Dr *[insert Doctors name]*

Patient *[insert Patients name]*

Identifier *[insert patient date of birth/address]*

I have received your request for shared care of this patient who has been advised to start *cinacalcet*

A I am willing to undertake shared care for this patient as set out in the protocol

B I wish to discuss this request with you

C I am unable to undertake shared care of this patient.

GP signature Date

GP address/practice stamp