Shared Care Guidance

Cinacalcet for the Treatment of Primary Hyperparathyroidism

This shared care agreement outlines the way in which the responsibilities for managing the prescribing of cinacalcet tablets for the treatment of primary hyperparathyroidism can be shared between the Secondary Care Specialist and the General Practitioner.

Cinacalcet is a calcimimetic that increases the sensitivity of the calcium-sensing receptor to activation by extracellular calcium. The drug's use has been approved by the North East Essex Medicines Management Committee and is designated an "Amber" medicine; one that requires secondary care specialist initiation and stabilisation prior to a primary care colleague taking over prescribing.

Indication:

Cinacalcet (Mimpara®) tablets are indicated for the reduction of hypercalcaemia in patients with primary hyperparathyroidism for whom parathyroidectomy would be indicated on the basis of serum calcium levels (as defined by relevant treatment guidelines), but in whom parathyroidectomy is not clinically appropriate or is contraindicated.(1)

Dose & Administration:

The recommended starting dose of cinacalcet 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.

Adverse Effects:

The most commonly reported adverse reactions are nausea and vomiting. Nausea and vomiting is usually mild to moderate in severity and transient in nature in the majority of patients.

Hypocalcaemia identified during cinacalcet therapy necessitates cessation of therapy and a direct referral to the secondary care specialist.

Dizziness, paraesthesia, reduced testosterone levels, rash, myalgia, asthenia are also commonly reported adverse effects; less frequently seizures, diarrhoea and dyspepsia occur.

Contraindications:

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- Hypersensitivity to cinacalcet or to any of the excipients included with the medicinal form.

Special warnings/precautions:

- Cinacalcet should only be used in pregnancy if potential benefit justifies potential risk to the foetus.
- It is not known whether cinacalcet is excreted in human milk and if breast feeding, careful benefit/risk assessment should be performed and a decision should be made to discontinue either breast-feeding or treatment with cinacalcet.
- Due to the potential for 2 to 4 fold higher plasma levels of cinacalcet in patients with moderate to severe hepatic impairment, the drug should be used with caution in these patients and treatment should be closely monitored, especially when making any dose increases.
- Cinacalcet treatment should not be initiated in patients with a serum calcium (corrected for albumin) below the lower limit of the normal range.
- Caution is advised in patients with risk factors for QT prolongation such as patients with known congenital long QT syndrome or patients receiving medicinal products known to cause QT prolongation.

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- The threshold for seizures is lowered by significant reductions in serum calcium levels and caution should be exercised in patients where this may be a risk.
- Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

Drug Interactions:

The cinacalcet Summary of Product Characteristics gives full details of the drug interactions associated with the treatment.(1)

Cinacalcet is metabolised in part by the enzymes CYP3A4; is a strong inhibitor of CYP2D6; and is partly metabolised by CYP1A2; therefore dose adjustments and careful prescribing may be required if a patient is taking concomitant therapy also metabolised by these enzymes.

Interactions with cinacalcet are listed below:

Ciprofloxacin	Ciprofloxacin is a CYP1A2 inhibitor and will increase the half-life of cinacalcet.
Dextromethorphan	Multiple doses of 50 mg cinacalcet increases the AUC of 30 mg dextromethorphan (metabolised primarily by CYP2D6) by 11-fold in CYP2D6 extensive metabolisers (interaction of minimal significance as dextromethorphan not widely used within practice).
Flecainide	Flecainide is metabolised by CYP2D6. Concomitant administration of cinacalcet will raise flecainide levels.
Fluvoxamine	Fluvoxamine is a CYP1A2 inhibitor and will increase the half-life of cinacalcet.
Itraconazole	Itraconazole is a CYP3A4 inhibitor which can cause a two fold increase in cinacalcet levels. On termination or initiation, dose adjustment of cinacalcet is required.
Ketoconazole	Ketoconazole is a CYP3A4 inhibitor which can cause a two fold increase in cinacalcet levels. On termination or initiation, dose adjustment of cinacalcet is required.
Metoprolol	Metoprolol is metabolised by CYP2D6. Concomitant administration of cinacalcet will raise metoprolol levels
Propafenone	Propafenone is metabolised by CYP2D6. Concomitant administration of cinacaclet will raise propafenone levels.
Rifampicin	Rifampicin is a CYP3A4 inducer and will reduce the half-life of cinacalcet.
Ritonanvir	Ritonavir is a CYP3A4 inhibitor which can cause a two fold increase in cinacalcet levels. On termination or initiation, dose adjustment of cinacalcet is required.
Smoking	Smoking induces CYP1A2 and reduces the half-life of cinacalcet. Close monitoring of the patient's smoking status is required and, if necessary, adequate adjustments of cinacalcet dosage made.
Tamoxifen	Concomitant administration of cinacalcet may reduce the levels of tamoxifen-avoid concomitant use.
Telithromycin	Telithromycin is a CYP3A4 inhibitor which can cause a two fold increase in cinacalcet levels. On termination or initiation, dose adjustment of cinacalcet is required.
Tricyclic antidepressants (desipramine, nortriptyline, clomipramine)	Tricyclic antidepressants are metabolised by CYP2D6. Concomitant administration of cinacalcet will raise the levels of these drugs.
Voriconazole	Voriconazole is a CYP3A4 inhibitor which can cause a two fold increase in cinacalcet levels. On termination or initiation, dose adjustment of cinacalcet is required.

Monitoring Requirements:

Serum calcium should be measured within 1-2 weeks after initiation or dose adjustment of cinacalcet (the SPC states within 1 week but local practice allows a little longer time). Once maintenance dose levels have been established, serum calcium should be measured every 3 months.; if clinically relevant reductions in serum calcium are not maintained, discontinuation of cinacalcet therapy should be considered.

Once the maintenance dose has been established, serum calcium should be measured approximately every 3 months.

Shared Care Responsibilities:

Secondary Care Specialist

1. Send a letter to the GP with Shared Care Guidelines requesting shared care for the patient.
2. Initiation of cinacalcet therapy and provision of therapy until the patient is stabilised on therapy.
3. Ensure that baseline monitoring is undertaken; ensuring that this information is communicated effectively to the Primary Care Practitioner.
4. To detail clearly in the patient's notes the reasons why the patient is unsuitable for surgery and clearly state these reasons in the correspondence to the Primary Care Practitioner when requesting that they participate in the Shared Care agreement.
5. Ensure that arrangements are made to monitor parathyroid hormone and bone profile every 3 months once a stable cinacalcet dose has been established. This will be monitored at 6 monthly hospital review and by the GP in between hospital visits.
6. Ensure the GP is copied in to the results of all monitoring
7. Discuss the benefits and side effects of treatment with the patient.
8. Report adverse events to the Medicines and Healthcare Products Regulatory Agency (MHRA). https://yellowcard.mhra.gov.uk/
9. Act promptly on any communication from GP colleagues requesting advice and support.
10. Promptly communicate the decision to discontinue therapy to the Primary Care Practitioner if on-going therapy is no longer thought to be beneficial.

Primary Care Practitioner

1. Submit letter of reply confirming acceptance.
2. Monitor patient's overall health and wellbeing.
3. Prescribe the drug treatment as described within this document.
4. Adjust the dose of cinacalcet (following initial stabilisation) in accordance with any future advice from the secondary care specialist.
5. Continue prescribing cinacalcet (once the required dose has been stabilised; usually between 4 and 12 weeks of therapy within secondary care); it is likely that cinacalcet therapy will be long term.
6. To undertake any necessary monitoring of the patient, including checking serum calcium levels every 3 months (between hospital visits); taking the required action in accordance with the below table; especially noting that if significant hypocalcaemia occurs, stop cinacalcet therapy and contact the secondary care specialist for further advice.

Monitoring Frequency	Results (S.Ca [corr])	Action
3 monthly	<2.2	Stop/reduce cinacalcet and refer back to the Secondary Care Specialist
	2.2 - 2.65	Dose adequate – continue treatment
	> 2.65	Refer to Secondary Care Specialist for review

7. Ensure the consultant is copied in to the results of all monitoring
8. Continually monitor patient's smoking status; if altered, discuss with Secondary Care Specialist.
9. Report to and seek advice from the Secondary Care Specialist on any aspect of patient care that is of concern and may affect treatment.

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10. Refer patient to the Specialist if his or her condition deteriorates.
11. Report any cinacalcet-related adverse events to the hospital specialist and MHRA.
12. Ensure that any new medication started is reviewed in terms of interactions with cinacalcet.
13. Inform prescribing clinician if smoking status changes.
14. Stop treatment on the advice of; after consultation with; the Secondary Care Specialist.

Patient (and if appropriate, the carer):

1. Report to the Secondary Care Specialist or GP if he or she does not have a clear understanding of the prescribed treatment.
2. Take the cinacalcet therapy in accordance with the prescribed instructions.
3. Attend GP surgery/hospital for all required blood testing and follow-up appointments.
4. Share any concerns in relation to treatment with cinacalcet.
5. Report any adverse effects to the Secondary Care Specialist or GP whilst taking cinacalcet therapy.

Contact Numbers for Advice and Support:

Colchester Hospital University NHS Foundation Trust	(01206) 747474 (Switchboard)
Consultant Endocrinologist:	
Dr Karunakaran Vithian	(01206) 742511 Karunakaran.Vithian@colchesterhospital.nhs.uk
CHUFT Pharmacy Department	***(***01206) 742355
CHUFT Medicines Information Help Line:	(01206) 742161

References

(1) Summary of Product Characteristics – Mimpara® (cinacalcet) 30mg, 60mg and 90mg film-coated tablets. Amgen Limited.
https://www.medicines.org.uk/emc/medicine/15432

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Section A (to be completed by Secondary Care Specialist):

Hospital Number:	
NHS No:	
Date:	
GP Courier No:	
GP Name:	

Name of patient:	
Date of Birth:	
Address:	

Background (including reasons why the patient is unsuitable for surgery and smoking status):

Medications:

Baseline Investigations:

Serum calcium before therapy:

Serum calcium 1 week after initiation:

U & Es:

Liver Function Tests:

Phosphate:

Dear GP,
See attached clinic letter. Please can you sign and return (using the above fax number) to indicate you are in agreement with the Shared Care Guidelines.

Yours sincerely,

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Section B (to be completed by General Practitioner):

The above patient has been accepted into our monitoring service.

Accepting GP Name:	
Accepting GP Signature:	
Date:	

Practice Stamp:

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