THE SHEFFIELD AREA PRESCRIBING GROUP

Shared Care Protocol

For

Cinacalcet for Primary Hyperparathyroidism in Adults

Shared care developed by:

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NHS Sheffield Clinical Commissioning Group
NHS Barnsley Clinical Commissioning Group
NHS Doncaster Clinical Commissioning Group
NHS Bassetlaw Clinical Commissioning Group
NHS Rotherham Clinical Commissioning Group
Sheffield Teaching Hospitals NHS Foundation Trust

Cinacalcet in Primary Hyperparathyroidism in Adults

Statement of Purpose

This shared care protocol (SCP) has been written to enable the continuation of care by primary care clinicians of patients initiated on cinacalcet for primary hyperparathyroidism by the Department of Endocrinology at Sheffield Teaching Hospitals, where this is appropriate and in the patients' best interests. Primary care will only be requested to take over prescribing of cinacalcet within its licensed indication unless specifically detailed otherwise below. Users should be aware that this document is guidance on the management of a condition, not a commissioning arrangement.

Responsibilities of specialist clinician

- To discuss benefits and side effects of treatment with the patient/carer and obtain informed consent, in line with national guidance. This is particularly important for unlicensed products.
- To provide patient / carer with contact details for support and help if required; both in and out of hours
- To initiate cinacalcet in appropriate patients
- To stabilise patient on a dose of cinacalcet with regular calcium monitoring
- To prescribe at least the first month's supply and until patient stable
- To contact patient's primary care prescriber to request prescribing and monitoring under shared care and send a link to or copy of the shared care protocol
- To advise the primary care prescriber regarding continuation of treatment, including the duration of treatment
- To discuss any concerns with the primary care prescriber regarding the patient's therapy
- The patient to remain under the specialists' care until the point of stopping medication

Responsibilities of the primary care clinician

- To refer appropriate patients to secondary care for assessment
- Confirm the agreement and acceptance of the shared care prescribing arrangement and that supply arrangements have been finalised (see appendix for template letter). Or To contact the requesting specialists if concerns in joining in shared care arrangements,
- To report any serious adverse reaction to the appropriate bodies eg: MHRA and the referring specialist
- To continue to prescribe for the patient as advised by the specialist
- Ensure monitoring as indicated in monitoring section below
- To inform the specialist if the patient discontinues treatment for any reason
- To seek the advice of the specialist if any concerns with the patient's therapy
- To conduct an annual medication review or more frequent if required.
- In the event that the primary care prescriber is not able to prescribe, or where the SCP is agreed but the specialist is still prescribing certain items e.g. Hospital only product; the primary care prescriber will provide the specialist with full details of existing therapy promptly by a secure method on request.
- For medication supplied from another provider prescribers are advised to follow recommendations for Recording Specialist Issued Drugs on Clinical Practice Systems

Responsibilities of Patients or Carers

- To be fully involved in, and in agreement with, the decision to move to shared care
- To attend hospital and primary care clinic appointments and to bring monitoring information eg: booklet (if required). Failure to attend will potentially result in the medication being stopped.
- Present rapidly to the primary care prescriber or specialist should the clinical condition significantly worsen
- Report any suspected adverse effects to their specialist or primary care prescriber whilst taking cinacalcet
- To read the product information given to them
- To take cinacalcet as prescribed
- Inform the specialist, primary care prescriber or community pharmacist dispensing their prescriptions of any other medication being taken – including over-the-counter medication

Indication

Cinacalcet is indicated for the treatment of hypercalcaemia in primary hyperparathyroidism for patients who are unsuitable / unfit / refuse parathyroidectomy and will avoid the need for further admission to hospital. 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.

For further information, please consult the NHS England Clinical Commissioning Policy for cinacalcet: https://www.england.nhs.uk/wp-content/uploads/2017/06/ccp-cinacalcet-complex-primary-hyperparathyroidism-adults.pdf

Selection of patients

Inclusions: Cinacalcet will be prescribed for the following patients:

(1) Who have first been discussed with the nominated lead clinician at the specialised endocrinology centre that provides services for patients with calcium and bone diseases;

AND

(2a) Who meet criteria for surgical intervention but who do not undergo surgery because they are unfit from a surgical or anaesthetic perspective or they refuse surgery, despite specialist input and clear counselling on the consequences of their decision;

OR

(2b) Who, following prior attempted parathyroidectomy, have residual or recurrent PHPT that is inaccessible or not amenable to further surgery;

AND

(3a) Are symptomatic with an adjusted serum calcium concentration between 2.85 - 3.00 mmol/L;

OR

(3b) Have biochemically severe hypercalcaemia (adjusted serum calcium >3.0 mmol/L);

AND

(4) Are vitamin D replete (>50nmol/L).

Exclusions: Cinacalcet will be not be routinely commissioned where:

(1) Adjusted serum calcium concentration is <2.85 mmol/L.

(2) Used in isolation to treat low bone mineral density. In this instance treatment with bisphosphonates are indicated.

(3) Used as sole treatment for PHPT where fracture risk is high, as cinacalcet does not reduce fracture risk.

(4) Prior to parathyroidectomy.

(5) Cinacalcet has previously been shown to be ineffective for that specific patient.

Dosage

The usual dose of cinacalcet is between 30-60mg twice daily. The calcium lowering effect is substantially present within two to three weeks (85-90%) after initiating therapy with 30mg twice daily. In patients whose adjusted calcium is not adequately controlled, the dose may be increased to a maximum of 90mg FOUR times daily.

Cinacalcet should be taken with or after food, preferably at the same time each day. Tablets should not be chewed or crushed.

Contra-indications

The details below are not a complete list and the current BNF and the SPC remain authoritative

Cinacalcet is contraindicated in:

- Known hypersensitivity to the drug or any of the excipients
- Pregnancy
- Breast-feeding
- Hypocalcaemia

Cinacalcet should be used with caution in:

- Epilepsy
- Moderate to severe hepatic insufficiency (Child-Pugh: Class B, C)
- Heart failure/ prolonged QT interval

Side –effects

The details below are not a complete list and the current BNF and the SPC remain authoritative

The most frequently reported adverse events are nausea and vomiting, rash, hypersensitivity, dizziness and myalgia. Isolated cases of hypotension, worsening heart failure and arrhythmia also reported.

Mild to moderate side effects e.g. nausea and vomiting are common and usually transient – GP to measure adjusted calcium, treat symptomatically and if symptoms persist to discuss with specialist.

Serious adverse events have occurred as a result of hypocalcaemia which are paraesthesias, myalgias, cramping, tetany and convulsions. QT prolongation and ventricular arrhythmia secondary to hypocalcaemia has also been reported – GP to measure adjusted calcium, stop cinacalcet and to discuss with specialist as soon as possible.

Monitoring

The aim of treatment is to maintain adjusted calcium at between 2.50 and 2.80 mmol/L.

Hospital Care

Baseline biochemical monitoring will be undertaken by the specialist. Adjusted calcium will be monitored 1 week after initiation or dose adjustment. Monitoring will continue under specialist care for 8 to 24 weeks until adjusted calcium levels are stable after dose titration based on adjusted calcium levels.
After transfer to GP care the patient will be reviewed yearly by specialist. Specialist to opportunistically arrange for calcium levels to be checked at annual clinic appointment.

GP Care

After maintenance dose has been established the patient's care will be handed over to GP who will then monitor adjusted calcium levels every 3 months for a year from commencing cinacalcet and if adjusted calcium levels are well controlled patient then to be monitored / checked every 6 months. This is based on evidence that after 6 months adjusted calcium levels should not be significantly changing (Luque-Fernandez 2013).
N.B. There may be a small number of patients where stabilisation will take 12 months or longer and these patients will therefore have the 3 monthly monitoring carried out in secondary care.

Actions

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

Adjusted Calcium level	Action for GPs
> 2.80mmol/L	Check compliance. Seek specialist advice as patient will require dose increase
2.20 – 2.50mmol/L	Check compliance. Seek specialist advice as patient will likely require dose reduction
< 2.20mmol/L	Stop cinacalcet, recheck adjusted calcium after 1 week.

	Seek specialist advice, likely resume at significantly lower dose

Interactions

The details below are not a complete list and the current BNF and the SPC remain authoritative

- **CYP2D6**
  Cinacalcet is a potential inhibitor of CYP2D6. Caution is advised with substrates of CYP2D6 as levels and side-effects may be increased (e.g. flecainide, metoprolol, tricyclic antidepressants).

- **CYP3A4**
  Cinacalcet is metabolised in part by CYP3A4. Co-administration with CYP3A4 inhibitors will cause an increase in cinacalcet levels. Co-administration with CYP3A4 inducers will cause a decrease in cinacalcet levels.
  Dose adjustment of Cinacalcet may be required if a patient initiates or discontinues therapy with a strong inhibitor (e.g. ketoconazole, itraconazole, telithromycin, voriconazole, ritonavir) or inducer (e.g. rifampicin, phenytoin, carbamazepine, phenobarbital).

- **CYP1A2**
  Cinacalcet is also metabolised by CYP1A2.
  Cautious use of ciprofloxacin (CYP1A2 inhibitor) is advised.
  Smoking induces CYP1A2 and therefore dose adjustments may be required if the patient starts or stops smoking during cinacalcet treatment.

- Warfarin is not affected by cinacalcet.

Additional information

Can be stored at room temperature; need to avoid excessive direct sunlight exposure.

Re-Referral guidelines

See monitoring and side effect sections

Ordering information

Cinacalcet is available through regular pharmaceutical wholesale chains.

Contacts for Support, education and information

Dr Miguel Debono
Endocrine Secretaries, B floor Royal Hallamshire Hospital, Glossop road, Sheffield S10 2JF

Endocrine Unit: 0114 271 3714

Medical Secretary: 0114 271 3175

References

Peacock, Munro; Bilezikian, J. P.; Bolognese, M. A.; Borofsky, Michael; Scumpia, Simona; Sterling, L. R.; Cheng, Sunfa; Shoback, Dolores. Cinacalcet HCl reduces hypercalcemia in primary hyperparathyroidism across a wide spectrum of disease severity. J. Clin. Endocrinol. Metab. 2011;96(1):E9-18.

Saponaro, Federica; Faggiano, Antongiulio; Grimaldi, Franco; Borretta, Giorgio; Brandi, Maria Luisa; Minisola, Salvatore; Frasoldati, Andrea; Papini, Enrico; Scillitani, Alfredo; Banti, Chiara; Del Prete, Michela; Vescini, Fabio; Gianotti, Laura; Cavalli, Loredana; Romagnoli, Elisabetta; Colao, Annamaria; Cetani, Filomena; Marcocci, Claudio. Cinacalcet in the management of primary hyperparathyroidism: post marketing experience of an Italian multicentre group. Clin. Endocrinol. (Oxf) 2013;79(1):20-26.

Inés Luque-Fernández, Antonia García-Martín and Alessandra Luque-Pazos Experience with cinacalcet in primary hyperparathyroidism: results after 1 year of treatment Ther Adv Endocrinol Metab 2013 4(3) 77– 81

Full list of side-effects is given in the Cinacalcet summary of product characteristics (SPC), available from www.emc.medicines.org.uk .

https://www.england.nhs.uk/wp-content/uploads/2018/03/responsibility-prescribing-between-primary-secondary-care-v2.pdf

It will be presumed by the referring specialist that the primary care team is operating under this shared care protocol. Should the primary care prescriber feel unable to act under this shared care protocol they should discuss with the specialist requesting the care in the first instance. If after discussion they still feel unable to prescribe then the primary care clinician must notify the specialist in writing.

Template letter to primary care prescriber

Dear Prescriber

RE: _____ DOB: ___/___/_____ NHS: _____

Address: _____ Postcode: _____

Your patient is being started on treatment with cinacalcet.

This treatment can be prescribed by primary care prescribers under the Traffic Light System under the "shared care" arrangements. This shared care protocol has been approved by the Sheffield Area Prescribing Group.

We have chosen to use cinacalcet because _____.

As part of shared care arrangements please can you monitor and prescribe for your patient as described above in the shared care protocol.

The next adjusted calcium blood test is due on…….

Please acknowledge you are happy to take on shared care by completing and returning the slip below to above address or by secure email to _____

Do not hesitate to contact us if you have any concerns.

Yours sincerely

Clinician's Name

Clinician's Title

IMPORTANT REMINDER

The prescriber is responsible for monitoring the patient on the medication being prescribed

RE: _____ DOB: ___/___/_____ NHS: _____

Address: _____ Postcode: _____

☐ I AGREE to take on shared care of this patient

☐ I DO NOT AGREE to take on shared care of this patient

Signed _____

Practice_____ Date_____