Approved by the Bedfordshire, Luton, and Milton Keynes Formulary Group (sub-committee of Area Prescribing Committee (APC), Sept 2021

SHARED CARE GUIDELINE

Cinacalcet for the management of PRIMARY hyperparathyroidism in patients with severe hypercalcaemia awaiting surgery or deemed unfit for surgical management

The following organisations contribute to and participate in the BLMK APC – Bedfordshire, Luton and Milton Keynes Clinical Commissioning Group; Bedfordshire Hospitals NHS Foundation Trust; Cambridgeshire Community Services NHS Trust; Central and North West London NHS Foundation Trust; East London NHS Foundation Trust; Milton Keynes University Hospital NHS Foundation Trust

SHARED CARE GUIDELINE

Cinacalcet for the management of PRIMARY hyperparathyroidism in patients with severe hypercalcaemia awaiting surgery or deemed unfit for surgical management

PATIENT NAME:		
ADDRESS:		
NHS NUMBER:		
CONSULTANT	NAME:	
TEL:	FAX:	EMAIL:
GP	NAME:	
TEL:	FAX:	EMAIL:
Other Health Care Professional contact details (if appropriate):		

The purpose of this template of principles for shared care is to provide a framework for the seamless transfer of care for a person from a hospital or specialist service setting to general practice, where this is appropriate and in their best interests.

Overview

- Primary hyperparathyroidism is a condition caused by over-activity of one or more of the four parathyroid glands and is a common endocrine condition. It is associated with increases in parathyroid hormone (PTH) levels and an increase in calcium and phosphate metabolism.
- Treatment with cinacalcet is recommended as an option by NICE (NICE guideline NG132) if surgery has been unsuccessful, is unsuitable or has been declined.
- Cinacalcet mimics the action of calcium on the parathyroid cells, suppressing PTH production
- Patients will be commenced on generic cinacalcet 30mg once daily. PTH and calcium will be monitored one, two and four weeks post initiation or following

dose adjustment by the hospital specialist and three monthly by the GP once established.
- Usual daily dose of cinacalcet is 30mg-180mg, taken orally, in one or two divided doses, with food or shortly after a meal. The maximum daily dose is 360mg.
- The most common adverse effects reported are nausea and vomiting
- Cinacalcet is metabolised in part through cytochrome P450 enzymes CYP3A4 and CYP1A2. Dose adjustment may be required if a patient receiving cinacalcet initiates or discontinues therapy with a strong inhibitor or inducer of CYP3A4
- Cinacalcet should not be used whilst breast-feeding. It should only be used in pregnancy if the potential benefit justifies the potential risk to the foetus.
- The responsibilities of the hospital specialist, GP and patient for this Shared Care Guideline can be found within this document.

N.B. Shared care arrangements can involve the Specialist Service sharing care with GPs or other health care professionals e.g. Community Nursing Service administering medicines subject to close monitoring. The same shared care principles apply.

- The hospital clinician/specialist service should prescribe if the patient will be attending hospital/specialist service regularly for specialist monitoring, otherwise contact the GP/other health care professional to agree to share care. It will be assumed that the GP/other health care professional will accept shared care unless they advise the hospital clinician/specialist service to the contrary.
- Transfer of clinical responsibility to primary care should only be considered where the person's clinical condition is stable or predictable.
- Patients should be at the centre of any shared care arrangements. Individual patient information and a record of their preferences (including patient consent) should accompany shared care prescribing guidelines where appropriate.
- A copy of the shared care guideline should be provided by the specialist centre initiating the treatment to both the patient (where appropriate) and the clinician participating in the shared care. Failure to provide a copy of the shared care guideline could result in a delay in responsibility for prescribing/administration being accepted in primary care.
- Adhere to CCG policies.
- The GP/other health care professional should have sufficient information on the drug to either allow them to monitor the patient's response to therapy and adjust dosages as required or know in what circumstances they should refer the patient back to the hospital clinician
- Where the hospital clinician/specialist service retains responsibility for monitoring drug therapy or making dosage adjustments, the GP/other health care professional must be informed of any dose changes as soon as possible to avoid an incorrect dose being administered. Similarly, if the GP/other health care professional changes the patient's medication then the hospital clinician/specialist service involved in the shared care agreement should be informed
- If a GP is unwilling to participate in a shared care agreement, the CCG medicines optimisation/management team should be asked for assistance in facilitating suitable prescribing arrangements for the patient.

- The patient should inform their usual community pharmacist that they will be starting the treatment to help ensure that supplies are available.

1. **A summary of the clinical condition**:

Primary hyperparathyroidism (PHPTH) is the third most common endocrine disorder with a prevalence of 6.72 per 1,000 and affects largely women. Removing abnormal parathyroid glands by surgery is the accepted treatment for PHPTH in a process known as a parathyroidectomy. The success rates of parathyroidectomy are high (about 97%) but not all patients will be suitable for surgery and some patients who undergo surgery may have some remaining disease or disease that keeps coming back - which is not suitable for further surgery. Some of these patients may be suitable for long-term observation - rather than surgery, however others need further therapy to manage symptoms of high calcium levels (hypercalcaemia).

The goals of treatment with cinacalcet for PHPTH are to lower levels of parathyroid hormone (PTH) and calcium in the blood, and to prevent or minimise the symptoms related to both elevated parathyroid hormone and calcium. Importantly cinacalcet does not reduce the risk of kidney stones or lower bone mineral density in patients with PHPTH and these issues must be separately addressed by the endocrinologist when considering the overall care of the patient. Cinacalcet should be used with caution in patients with a history of kidney stones due to higher risk with increased calcium excretion.

Cinacalcet is described as a calcimimetic because it mimics the action of calcium, and can bind and activate the calcium receptors on parathyroid cells, thus suppressing the production of PTH.

Cinacalcet is not recommended for the routine treatment of patients with HPTH and surgery remains fist line treatment for those who are suitable for treatment.

In 2008, cinacalcet was approved by the European Medicines Agency (EMA) for patients with PHPTH indicated for parathyroidectomy on the basis of serum calcium levels, but for whom surgery was contraindicated or clinically inappropriate. Cinacalcet is recommended for the treatment of PHPTH in patients who are not deemed suitable for parathyroid surgery with serum calcium:

a) >2.85mmol/l and patients have symptoms related to hypercalcaemia
b) >3.0mmol/l regardless of symptoms

Response to treatment should be monitored regularly and treatment should be continued only if a reduction in the plasma levels of intact parathyroid hormone of 30% or more is seen within four months of treatment, including dose escalation as appropriate.

2. Details of the drug therapy:

- Cinacalcet will be commenced by the endocrine consultant at a dose of 30mg, taken orally, once daily.
- The dose will be adjusted as required to achieve the calcium level within the target range <2.8mmol/L.
- If calcium has not fallen by a minimum of 0.25mmol/L in the first eight weeks the dose of cinacalcet should be increased to 30mg, taken orally, twice daily The usual daily dose of cinacalcet is 30mg-180mg in divided doses but can go up to 360mg per day.
- Cinacalcet should be swallowed whole, with food or shortly after a meal as this increases bioavailability.
- Generic cinacalcet should be prescribed

Further information can be found in the Summary of Product Characteristics.

Cautions

- Cinacalcet is not at effective at reducing the end organ damage caused by PHPTH including reduced bone mineral density leading to osteopenia and osteoporosis and hypercalcuria which can cause renal stones. These risks must be managed separately
- Significant reductions in serum calcium levels can lead to paraesthesias, myalgias, cramping, tetany and convulsions, and QT-interval prolongation and ventricular arrhythmias. Therefore cinacalcet is cautioned in patients with known congenital long QT syndrome or patients receiving medicinal products known to cause QT prolongation.
- Moderate-severe hepatic impairment (Child-Pugh classification) due to the potential for 2 to 4-fold higher plasma levels of cinacalcet and risk of hypocalcaemia.

Contraindications

- Hypocalcaemia.
- Hypersensitivity to the active substance or any of the excipients.
- Safety and efficacy have not been established in patients below the age of 18 years.
- Cinacalcet should only be used in pregnancy if the potential benefit justifies the potential risk to the foetus. It should not be used whilst breast-feeding.

Interactions

- Concurrent administration of other medicinal products known to reduce serum calcium may result in an increased risk of hypocalcaemia.
- Cinacalcet is metabolised in part through cytochrome P450 enzymes CYP3A4 and CYP1A2.
    - Dose adjustment may be required if a patient receiving cinacalcet initiates or discontinues therapy with a strong inhibitor (e.g. azoles, telithromycin, ritanovir) or inducer (e.g. rifampicin) of CYP3A4.
    - Smoking induces CYP1A2 and clearance of cinacalcet is higher in smokers than non-smokers.

    - The effect of CYP1A2 inhibitors (e.g. fluvoxamine, ciprofloxacin) is not known but may impact on dosage if these drugs are discontinued or initiated.
- Cinacalcet is a strong inhibitor of CYP2D6. Dose adjustments of concomitant medicinal products may be required when cinacalcet is administered with individually titrated, narrow therapeutic index substances that are predominantly metabolised by CYP2D6 (e.g. flecainide, propafenone, metoprolol, desipramine, nortriptyline, clomipramine).

NICE guideline (NG132) titled Hyperparathyroidism (primary): diagnosis, assessment and initial management recommends considering cinacalcet for people with primary hyperparathyroidism if surgery has been unsuccessful, is unsuitable or has been declined, and if their albumin-adjusted serum calcium level is either:

2.85 mmol/litre or above with symptoms of hypercalcaemia or
3.0 mmol/litre or above with or without symptoms of hypercalcaemia.

For people whose initial albumin-adjusted serum calcium level is 2.85 mmol/litre or above with symptoms of hypercalcaemia, base decisions on whether to continue treatment with cinacalcet on how well it reduces symptoms.

3. Details of possible adverse effects and actions to be taken.

In controlled studies the most common adverse effect reported were GI disturbance with nausea and vomiting, in most cases this was mild to moderate in severity and transient in nature.

Another significant problem is hypocalcaemia which has been linked to an increased risk of seizure, paraesthesia and QT-interval prolongation.

Very common (≥ 1 in 10)
- Nausea
- Vomiting

Common (≥ 1 in 100 and < 1 in 10)
- Hypersensitivity reactions (angioedema and urticaria)
- Rash
- Anorexia
- Dizziness
- Dyspepsia
- Myalgia
- Asthenia
- Reduced testosterone levels

Further information can be found in the Summary of Product Characteristics.

4. Monitoring instructions and responsibilities

Calcium should be monitored one week, two weeks and four weeks post initiation or following dose adjustment by the hospital specialist.

- Once calcium is in the target range on a stable dose of cinacalcet the GP should monitor calcium every three months.
- Once stabilised on cinacalcet acute derangements in calcium are rare with the exceptions of poor compliance with cinacalcet or clinical dehydration.
- The GP should seek advice from the hospital specialist if calcium falls <2.4mmol/L or rises >2.8mmol/L. The patient should continue to take cinacalcet unless exhibiting symptoms of hypocalcaemia, or calcium is less than 2.2mmol/L

a. Hospital specialist team:

- Initiate cinacalcet: prescribe/adjust the dose of cinacalcet until calcium is within the target range <2.8mmol/L.
- Arrange blood tests during the initiation of cinacalcet whilst being prescribed by the hospital.
- Organise the supply of medication to the patient, whilst cinacalcet is being initiated until prescribing is transitioned to the GP.
- Send a letter to the GP requesting shared care for the patient.
- Inform the GP after each clinic attendance if there is any change to treatment or monitoring and patients who do not attend clinic appointments.
- To provide any advice to the patient/carer when requested.
- Provide a follow up appointment with the patient every 12 months after transitioned to GP prescribing.

b. General practitioner:

- Agreement to shared care guideline by the GP.
- Prescribe cinacalcet at the dose advised by the hospital specialist.
- Check serum calcium every three months and seek advice from the hospital specialist if calcium falls <2.4mmol/L or rises >2.8mmol/L.
- Report any adverse events to the hospital specialist and request advice from the hospital specialist when necessary.
- Monitor smoking status of patient and seek guidance from specialist if this changes (smoking reduces plasma levels of cinacalcet). Explain the effect of smoking on therapy and encourage smokers to quit.

5. Patient Responsibilities.

- Report to the hospital specialist or GP if they do not have a clear understanding of their treatment.
- Patients must not exceed the recommended dose.
- Patients must attend their scheduled clinic and blood test appointments (where relevant).
- Must inform other clinical staff that they are receiving treatment.
- Report any adverse effects to the hospital specialist or GP.

- Attempt to cease smoking and notify any change in smoking status to GP/ specialist.

6. Community Pharmacists Responsibilities

- Know where to access locally agreed shared care guidelines to aid professional clinical check of prescription prior to dispensing.
- Professionally check prescriptions to ensure they are safe for the patient and contact the Primary Care prescriber if necessary to clarify their intentions.
- Fulfil legal prescriptions for medication for the patient unless they are considered unsafe.
- Counsel the patient on the proper use of their medication.
- Advise patients suspected of experiencing an adverse reaction to their medicines to contact their Primary Care prescriber or Specialist/Specialist nurse team.

7. Contact details of Specialist unit (for any queries, and advice regarding frequency of ongoing specialist service review)

Bedford Hospital
Consultants:
Dr Alison Melvin
Dr Mustafa Khan
Dr Rajeev Kumar
Dr Shwe Pan

Telephone: 01234 792287
Fax: 01234 792180

Luton & Dunstable Hospital
Consultants
Dr Shiu-Ching Soo - 01582 497564
Dr Rehman – 01582 497202
Dr Banerjee – 01582 497204
Dr Naziat – 01582 497204

Milton Keynes Hospital

Dr Asif Ali - 01908 660033 ext 87106
Dr Asif Humayun - ext 87122
Dr Shanthi Chandran - ext 87094

7. References

NICE guideline (NG132) titled Hyperparathyroidism (primary): diagnosis, assessment and initial management Published May 2019

Cinacalcet 30mg tablets Summary of product characteristics (Aurobindo Pharma - Milpharm Ltd). Accessed on www.medicines.org.uk on 30th June 2021.