NHS LINCOLNSHIRE in association with
UNITED LINCOLNSHIRE HOSPITALS TRUST

SHARED CARE GUIDELINE: CINACALCET in the management of secondary hyperparathyroidism in adult patients with end-stage renal disease on dialysis and hypercalcaemia of primary hyperparathyroidism or parathyroid carcinoma.

General Principles

Shared Care Responsibilities:
In its guidelines on responsibility for prescribing (circular EL (91) 127) between hospitals and general practitioners, the Department of Health has advised that legal responsibility for prescribing lies with the doctor who signs the prescription. (BNF, 66, September - March 2014, p. 5)
Aims:
(1) The aim of shared care guidelines is to provide information and/or guidance to GPs and hospital staff relating to the potentially complex implications of sharing patient care for a specific drug between primary and secondary/tertiary care.
(2) Specific shared care guidance should be available for any high cost or high-risk drug therapy or device that may be prescribed for a patient following specialist referral. Such guidance will only be produced where shared care is considered an appropriate option.
(3) Each guideline will include a clear statement of the responsibilities of both the GP and the specialist unit within the overall provision of the treatment to the patient.
(4) Shared care guidelines will ensure that the GP has sufficient information available to undertake to prescribe a specialist treatment if s/he so wishes. It is not the intention of these guidelines to insist that GPs prescribe such treatment and any doctor who does not wish to accept clinical or legal responsibility to prescribe such a drug is under no obligation to do so. Nonetheless the development of a shared care guideline will only be undertaken within the context of a broad acceptance between Lincolnshire Prescribing and Clinical Effectiveness Forum (PACEF) and secondary/tertiary care that GP prescribing of such a treatment is appropriate within the constraints of formal shared care. Any drug approved for the development of a shared care guideline will automatically be classified as amber on the Lincolnshire Traffic Lights List and, if high-cost, will be supported financially through the High Cost Drugs Reserve. Thus there should be no financial reason why a GP should be deterred from prescribing a high cost drug under a shared care guideline.

Further copies

Further copies of any guideline in this series are available from members of the Greater East Midlands Commissioning Support Unit (GEMS) Prescribing & Medicines Optimisation Team.

Date of Issue: October 2015
Review Date: October 2017

Lincolnshire East CCG
Lincolnshire West CCG
South Lincolnshire CCG
South West Lincolnshire CCG
Lincolnshire Partnership Foundation Trust
United Lincolnshire Hospitals Trust
Greater East Midlands Commissioning Support Unit

Drug Details
Approved Name: **Cinacalcet**
Brand Name: Mimpara
Form and Strength: Tablets 30, 60 and 90mg

General Medical Council (GMC) - Good Practice In Prescribing And Managing Medicines and Devices which came into effect 25th February 2013 states
Good practice recommendation 43
If you are uncertain about your competence to take responsibility for the patients continuing care you should seek further information or advice from the clinician with whom the patient's care is shared or from another experienced colleague. If you are still not satisfied you should explain this to the other clinician and to the patient and make appropriate arrangements for their continuing care

Specialist Responsibilities
The specialist secondary/tertiary care service will:
1. Send a letter to the GP suggesting that shared care is agreed for this patient.
2. Ensure that the patient receives supplies of cinacalcet from the hospital or prescribed on FP10HP until the GP formally agrees to share care.
3. Carry out baseline U&Es, calcium, phosphate and parathyroid hormone (PTH) levels in line with local and national guidelines/protocols.
4. Check current smoking status before commencing therapy and continue routine monitoring once commenced on treatment.
5. Initiate and adjust the dose of cinacalcet as necessary according to clinical response.
6. Provide patient with pre-treatment information leaflet.
7. Communicate promptly any changes in biochemistry monitoring and modification of cinacalcet dose to the GP.
8. Periodically (at one to six monthly intervals in clinic) review the patient's clinical condition.
9. Have a mechanism in place to receive rapid referral of a patient from the GP in the event of deteriorating clinical condition.
10. Follow up any adverse drug reactions reported by the GP and report back to the GP.
11. Advise the GP in stopping treatment.

GP Responsibilities

The GP will:

1. Notify the consultant in writing, within two weeks, if they agree to share care.
2. Monitor the patients overall health and wellbeing.
3. Monitor the patient for adverse drug reactions and remain vigilant to the risk of potential drug interaction.
4. Carry out any investigations that are communicated and deemed appropriate.
5. Provide repeat prescriptions according to recommendations on dosage by the renal unit, Lincoln County Hospital.

Referral Criteria

Renal patients

1. Patients will have been stabilised on their Vitamin D analogues and phosphate binders.
2. The specialist will have carried out an assessment of efficacy.
3. Patients will be stabilised on cinacalcet.

Endocrinology patients

1. The specialist will have carried out an assessment of efficacy.
2. Patients calcium levels will be stabilised on cinacalcet therapy .

Licensed Indications

Cinacalcet is licensed for the treatment of secondary hyperparathyroidism in adult patients over 18 years with end-stage renal disease (ESRD) on maintenance dialysis.

Cinacalcet is licensed for the treatment of hypercalcaemia of primary hyperparathyroidism or parathyroid carcinoma.

Recommended Dosage and Administration

Renal patients

Initially 30mg once daily, adjusted every 2 to 4 weeks to a maximum of 180mg daily, to achieve a target level of intact PTH of between 15.9 and 31.8 pmol/litre.

Cinacalcet should be taken with food or shortly after a meal, as studies have shown that bioavailability of cinacalcet is increased when taken with food.

Tablets should be taken whole and not divided.

For use only in patients who have plasma levels of intact parathyroid hormone greater than 85 pmol/litre that are refractory to standard therapy, and a normal or high adjusted serum calcium level **and** in whom surgical parathyroidectomy is contraindicated, in that the risks of surgery are considered to outweigh the benefits.

Endocrinology patients

Adult patients initially 30mg twice daily adjusted every two to four weeks according to response up to a maximum of 90mg four times a day.

Normal Maintenance dose range 30mg twice daily to 60mg twice daily[5].

Lincolnshire East CCG
Lincolnshire West CCG
South Lincolnshire CCG
South West Lincolnshire CCG
Lincolnshire Partnership Foundation Trust
United Lincolnshire Hospitals Trust
Greater East Midlands Commissioning Support Unit

Background Pharmacology

Cinacalcet is a calcimimetic agent which increases the sensitivity of calcium-sensing receptors to extracellular calcium ions, thereby inhibiting the release of PTH. It is licensed for the treatment of secondary hyperparathyroidism in patients with ESRD on maintenance dialysis therapy. It may be used as part of a therapeutic regimen including phosphate binders and/or Vitamin D sterols, as appropriate.

Preparations Available

30, 60 and 90 mg film coated tablets.

Adverse Effects

Most commonly reported adverse effects are nausea and/or vomiting which occur in around 30% of patients normally mild to moderate in severity and transient in nature in majority of patients. Other common adverse effects are anorexia, dizziness, paraesthesia, asthenia, rash, myalgia and reduced testosterone levels.
Less commonly dyspepsia, diarrhoea and seizures; hypotension, heart failure and allergic reactions (including angioedema). For full list of reported adverse effects refer to SPC.

Drug Interactions

The BNF highlights one drug interaction of potential clinical significance.
Cinacalcet possibly inhibits the metabolism of tamoxifen to its active metabolite and therefore concomitant use should be avoided.
Other drug interactions which are detailed within the products SPC are:
Antifungals – metabolism of cinacalcet inhibited by ketoconazole leading to increased plasma concentrations. Manufacturer also advises caution if concomitant use of itraconazole or voriconazole is required.
Cinacalcet is in part metabolised by CYP3A4 enzyme. Inhibitors of this enzyme such as ritonavir or telithromycin, or an inducer (e.g. rifampicin) may also affect serum levels and dose adjustment of cinacalcet may be necessary.
Tobacco – metabolism of cinacalcet increased by tobacco smoking leading to reduced plasma concentrations. Recommended dose adjustment may be needed if smoking started or stopped during treatment.
Medicinal products metabolised by the enzyme P450 2D6 (CYP2D6):
Cinacalcet is a strong inhibitor of CYP2D6. Manufacturer advises that dose adjustments of concomitant medicinal products may be required when Mimpara is administered with individually titrated, narrow therapeutic index substances that are predominantly metabolised by CYP2D6 (e.g. flecainide, propafenone, metoprolol given in heart failure, desipramine, nortriptyline, clomipramine).

Precautions and Contraindications

Precautions

Cinacalcet treatment should not be initiated in patients with hypocalcaemia.
For renal patients this is serum calcium (corrected for albumin) below the lower limit of the normal range.
Since cinacalcet lowers serum calcium, patients should be monitored carefully for the occurrence of hypocalcaemia.
Liver impairment. – Manufacturer advises caution in moderate to severe impairment, monitor closely especially when increasing dose.
Pregnancy – Manufacturer advises should only be used during pregnancy if the potential benefit justifies the potential risk to the foetus.

Contraindications

Breast feeding Manufacturer advises avoid as cinacalcet present in milk in animal studies.

Monitoring

Renal patients

Baseline:

Measure serum calcium levels within one week of starting treatment or adjusting dose, then every one to three months.
Blood levels of U&Es, calcium and phosphate monthly or at each clinic visit, parathyroid hormone levels every 3 months.
Following dose adjustment serum calcium levels should be monitored within the week and parathyroid hormone levels should be monitored every 4 weeks following dose changes.
Dose adjustment may be necessary if smoking started or stopped during treatment.
If Parathyroid Hormone levels fall to within normal range, the dose of cinacalcet should be reviewed.

All monitoring is the responsibility of the renal services (see specialist responsibilities on page 2).

The specialist renal services also have the responsibility of ensuring the GP who has assumed the prescribing responsibility for cinacalet is made aware promptly of all test results and any subsequent changes to therapy.

Endocrinology patients

Baseline:

Measure serum calcium levels within one week of starting treatment or adjusting dose, then every one to three months.
Blood levels of U&Es, calcium and phosphate monthly or at each clinic visit, parathyroid hormone levels every 3 months.
Once prescribing responsibility transferred back to GP GP to monitor bone profile 6 monthly

Treatment should be reviewed and advice from the supervising specialist sought if:

Any component of bone profile falls outside of normal range .

Following dose adjustment serum calcium levels should be monitored within the week and parathyroid hormone levels should be monitored every 4 weeks following dose changes.
Dose adjustment may be necessary if smoking started or stopped during treatment.

Lincolnshire East CCG
Lincolnshire West CCG
South Lincolnshire CCG
South West Lincolnshire CCG
Lincolnshire Partnership Foundation Trust
United Lincolnshire Hospitals Trust
Greater East Midlands Commissioning Support Unit

If Parathyroid Hormone levels fall to within normal range, the dose of cinacalcet should be reviewed.

All patients

Treatment should be reviewed and advice from the supervising specialist sought if:

- **There is deterioration in the clinical condition and/or the patient experiences major**

Side-effects.

- Adjusted serum calcium levels fall outside the range of 2.2 to 2.6mmol/l.

Indication of Likely Cost of Therapy in Primary Care

Cinacalcet 30mg tablets £125.75 for 28 tablets, 28 x 60mg = £231.97, 28 x 90mg = £347.96(all ex VAT)

Information Given to the Patient

Patient information leaflet available with each container of cinacalcet.

Contact Details Renal physicians

Consultant Nephrologists

Dr Little's Secretary: 01522 573961
Dr Malik's Secretary: 01522 572335
Dr Williams' secretary: 01522 572335

Renal Pharmacist

Caroline Taylor: 01522 573598
Renal Pharmacist
County Hospital

Contact details endocrinologists

Lincoln County Hospital

Dr Ravikumar
Dr Desilva
Dr Sriraman

Pilgrim Hospital

D D Eapen 01205 446499
Dr A Tarik 01205 446499
Dr K Jacob 01205 446718

References

1. BNF 66, September - March 2014.
2. SPC Mimpara Amgen Ltd. Last updated 24/10/2013, accessed at eMC website 29th January 2014.
3. Leicestershire Medicines Strategy Group. Full shared care agreement for Cinacalcet in the treatment of Secondary Hyperparathyroidism. Approved February 2012. next review February 2015.
4. North of Tyne Shared care Group. Shared care guidelines for the use of cinacalcet in primary hyperparathyroidism. January 2013.
5. Cinacalcet efficacy in patients with moderately severe primary hyperparathyroidism according to the European Medicine prescription handling. Cetani F, Saponcro F et al. J Endocrinol Invest 2012 Jol : 35(7) 655-660

Author(s)

Caroline Taylor, Renal Pharmacist, United Lincolnshire Hospital Trust
Cathy Johnson, Interface Lead Pharmacist, NHS Lincolnshire