NHS LINCOLNSHIRE in association with
UNITED LINCOLNSHIRE HOSPITALS TRUST

SHARED CARE GUIDELINE: CINACALCET treatment of hypercalcaemia in parathyroid carcinoma, and the treatment of primary hyperparathyroidism in patients where parathyroidectomy is inappropriate.

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, 76, September 18 - March 2019, 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 Optum Health System Support (HSS), Medicines Management and Optimisation (MMO) Team.

Date of Issue: March 2019
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Principles of shared care

NHS England published Guidance - Responsibility for prescribing between Primary, Secondary and Tertiary care – January 2018.

Extracts from guidance highlighting the key recommendations:
(Numbering kept from original document, for reference)

1.0 Introduction

1.1 Shared Care Prescribing guidelines are local policies to enable General Practitioners to accept responsibility for the prescribing and monitoring of medicines/ treatments in primary care in agreement with the initiating service.

1.4 Where possible shared care should be disease specific rather than medicine specific and link into complement local integrated care pathways and shared care policies. Medicines and conditions suitable for shared care will be identified by local medicines committees and will be classified as AMBER (AMBER 1 for Lincolnshire) through the traffic light system.

… However it should be remembered that the provision of shared care prescribing guidelines does not necessarily mean that the GP has to agree to accept clinical and legal responsibility for prescribing; that they should only do so if they feel clinically confident in managing that condition.

2.3 Reasonable predictable clinical situation

2.3.1 Transfer of clinical responsibility to primary care should only be considered where the person's clinical condition is stale or predictable.

2.4 Agreement of shared care between consultant and GP

2.4.1 Referral to the GP should only take place once the GP has agreed in each individual case and the hospital or specialist will continue to provide prescriptions until a successful transfer of responsibilities. The GP should confirm the agreement and acceptance of the shared care prescribing arrangement and that the supply arrangements have been finalised. The secondary/ tertiary provider must supply an adequate amount of the medication to cover the transition period. The patient should then be informed to obtain further prescriptions from the GP.

2.7 Clear definition of responsibility

2.7.1 The areas of care for which each clinician has responsibility should be clearly defined.

2.8 Clinical responsibility

2.8.1 Clinical responsibility for prescribing is held by the person signing the prescription who must also ensure adequate monitoring.

2.9 Communication network & emergency support

2.9.1Telephone details and (if appropriate) secure email addresses of both parties should be exchanged and recorded. This will enable the practice to access timely advice, guidance and information if problems arise, and will also enable secondary care clinicians to easily contact the GP if necessary. This should include out of hours contact numbers, how to access the on-call duty doctor. Patients and their carers should also be provided with contact details for support and help if required both in and out of hours.

2.9.2 People who are being treated on the advice of a secondary care team, but are no longer being seen in that setting, may still need a review should problems arise. The appropriate level of care or advice should be available from the secondary care team in a timely manner without necessarily requiring a new referral.

6.0 Monitoring

6.0.1 All appropriate monitoring arrangements must be fulfilled. The person delivering that aspect of the shared care agreement should ensure that the resources to do this are in place in the clinical setting in which they are delivered.

Drug Details

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

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 specialist.

Referral Criteria

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 patients with end-stage renal disease (ESRD) on maintenance dialysis.
Cinacalcet is licensed for the treatment of hypercalcaemia in parathyroid carcinoma. It is also licensed for treatment of primary hyperparathyroidism in patients where parathyroidectomy is inappropriate.

Recommended Dosage and Administration

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].

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

For further information on adverse effects please refer to the online BNF which can be accessed via https://bnf.nice.org.uk/
or from the Summary of Product Characteristics which can be accessed via: www.medicines.org.uk
Common or very common – appetite decreased, asthenia, back pain, constipation, diarrhoea, dizziness, dyspnoea, electrolyte imbalance, gastrointestinal discomfort, headache, hypersensitivity, hypotension, muscle complaints, nausea, paraesthesia, rash, seizure, upper respiratory tract infection, vomiting.
Frequency not known – heart failure aggravated, osteodystrophy, QT interval prolongation, tetany, ventricular arrhythmia.

Drug Interactions

For detailed information on drug interactions, please refer to the online BNF which can be accessed via https://bnf.nice.org.uk/
or from the Summary of Product Characteristics which can be accessed via: www.medicines.org.uk
Below is a summary of some of the key interactions.
Medicines known to reduce serum calcium – co-administration with cinacalcet may result in increased risk of hypocalcaemia. Patients receiving cinacalcet should not be given etelcalcetide.
CYP3A4 enzyme inhibitors – ketoconazole, itraconazole, telithromycin, voriconazole, and ritonavir can increase cinacalcet levels and dose adjustments may be necessary.
CYP3A4 enzyme inducers - may affect cinacalcet levels and dose adjustment may be necessary.

Cinacalcet possibly inhibits the metabolism of tamoxifen to its active metabolite and therefore concomitant use should be avoided.
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 cinacalcet is administered with individually titrated, narrow therapeutic index substances that are predominantly metabolised by CYP2D6 (e.g. flecainide, propafenone, metoprolol, desipramine, nortriptyline, clomipramine).

Precautions and Contraindications

For further information on contraindications and cautions in use, please refer to the online BNF which can be accessed via https://bnf.nice.org.uk/
or from the Summary of Product Characteristics which can be accessed via: www.medicines.org.uk

Contraindications
Hypersensitivity to cinacalcet or to any of the excipients.
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.
Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose- galactose malabsorption should not take this medicine.
Breast feeding Manufacturer advises avoid as cinacalcet present in milk in animal studies.

Precautions
Since cinacalcet lowers serum calcium, patients should be monitored carefully for the occurrence of hypocalcaemia. Manifestations of hypocalcaemia may include paraesthesia's, myalgia's, cramping, tetany and convulsions.
Decreases in serum calcium can also prolong QT interval potentially resulting in ventricular arrhythmia secondary to hypocalcaemia. Caution should be advised in patients with other risk factors for QT prolongation such as those with known congenital long QT syndrome or patients receiving medicines known to cause QT prolongation.
Liver impairment. – Manufacturer advises caution in moderate to severe impairment, monitor closely especially when increasing dose.
Seizures- cases of seizures have been reported with patients treated with cinacalcet. The threshold for seizures is lowered by significant reductions in serum calcium levels. Therefore calcium levels should be closely monitored in patients with a history or seizure disorder.
Hypotension and or worsening heart failure - cases have been reported in patients with impaired cardiac function receiving cinacalcet.
Pregnancy – Manufacturer advises should only be used during pregnancy if the potential benefit justifies the potential risk to the foetus.

Monitoring

Endocrinology patients
Baseline:
Measure serum calcium levels before initiation of treatment and within one week of starting treatment or adjusting dose, then every two 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.
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 adverse 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 (Drug Tariff April 2019)

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

Information Given to the Patient

Patient information leaflet available with each container of cinacalcet.

Contact Details Renal physicians

Contact details endocrinologists
Lincoln County Hospital
Dr Ravikumar
Dr Desilva
Dr Sriraman
Pilgrim Hospital
Dr D. Eapen 01205 446499
Dr A. Tarik 01205 446499

References

1. BNF 76 September 2018 - March 2019 and https://bnf.nice.org.uk/
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

Additional references used in 2019 review

6. BNF accessed online March 2019
7. Emc. Mimpara tablets . (Amgen ltd. Last updated 4th September 2017.

Author(s) for Original protocol which included use for renal indications

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