South West Yorkshire Partnership NHS Foundation Trust | Barnsley Hospital NHS Foundation Trust | Barnsley Clinical Commissioning Group

Sodium Clodronate (Bonefos)

Shared Care Guideline for the treatment and prevention of bone disease in multiple myeloma.

Introduction

Indication/Licensing information

Oral sodium clodronate is indicated for the management of osteolytic lesions, hypercalcaemia and bone pain associated with skeletal metastases in patients with multiple myeloma. It is also indicated for the maintenance of clinically acceptable serum calcium levels in patients with hypercalcaemia of malignancy initially treated with an intravenous bisphosphonate.

- Bisphosphonate therapy is recommended for all patients with symptomatic multiple myeloma, whether or not bone lesions are evident
- There is no consensus regarding the duration of bisphosphonate therapy. The standard of care to date has been indefinite bisphosphonate therapy. However, given the risk of bisphosphonate related osteonecrosis of the jaw (BONJ), it is reasonable to consider stopping therapy under certain circumstances such as those patients who have achieved a complete response/very good partial response and have no active bone disease; this should be at the discretion of the treating haematologist.
- At present there is insufficient evidence to make a recommendation for the use of bisphosphonates in patients with asymptomatic myeloma

Pharmacology

Clodronate is a bisphosphonate which have been shown, *in vitro*, to inhibit the formation and dissolution of calcium phosphate (hydroxyapatite). *In vivo*, they have been shown to inhibit bone resorption to a greater or lesser extent, depending on the compound , and clodronate is one of the most effective in this respect.

Dosage and administration

- Dose: 1.6 g daily in 1–2 divided doses, then increased if necessary up to 3.2 g daily (short term) in 2 divided doses. Swallow whole with a glass of water. Use of the divided dose regimen rather than a single daily dose may improve gastro-intestinal tolerance.
- Avoid food for 2 hours before and 1 hour after treatment, particularly calcium-containing products e.g. milk, oral calcium and vitamin D supplements; also avoid iron and mineral supplements and antacids; maintain adequate fluid intake
- Available as 800mg tablets

Dosage in renal impairment

Degree of renal failure	Creatinine Clearance, ml/min	Dose
Mild	50-80 ml/min	1600 mg daily (no dose reduction recommended)
Moderate	30-<50 ml/min	1200 mg/daily
Severe	10-30 ml/min	800 mg/daily

Prescriber Responsibilities:

Responsibilities of the specialist initiating treatment

Summary

- To assess the suitability of the patient for treatment.
- To discuss the benefits and side effects of treatment with the patient/carer and the need for long term monitoring if applicable.
- To prescribe for the first 12 weeks of sodium clodronate treatment.
- To perform baseline tests and if appropriate routine tests until the patient is stable.
- To ask the GP whether they are willing to participate in shared care.
- To provide the GP with a summary of information relating to the individual patient to support the GP in undertaking reduced shared care (See Shared care request form in Appendix A).
- To advise the GP of any dosage adjustments required, monitoring required, when to refer back, and when and how to stop treatment (if appropriate).
- To monitor the patient for adverse events and report to the GP and where appropriate Commission on Human Medicines/MHRA (Yellow card scheme).
- To provide the GP with contact details in case of queries.

Baseline Tests
Renal function, liver function, U&Es, serum calcium and phosphate levels

Routine Tests
Renal function, liver function, U&Es, serum calcium and phosphate levels

Disease monitoring
Routine tests should take place every 4 weeks initially, stepped down to every 3 months when treatment is stable and GP requested to take on shared care. The patient will be reviewed by the specialist every 4 months.

Responsibilities of other prescribers

Acceptance of Responsibility by the Primary Care Clinician
It is optional for GPs to participate in taking on responsibility for shared care for the patient. GPs will take on shared care only if they are willing and able.

Summary

- To reply to the request for shared care as soon as possible.
- To prescribe and adjust the dose as recommended by the specialist.
- To ensure there are no interactions with any other medications initiated in primary care.
- To continue monitoring as agreed with secondary care (guideline should include details of monitoring requirements and what to do when each of the defined parameters alters).
- To refer back to the specialist where appropriate. For example:
  - Patient or general practitioner is **not** comfortable to continue with the existing regime due to either change in condition or drug side effects.
  - Advice in respect of concordance.
- Discontinue the drug as directed by the specialist if required
- To identify adverse events if the patient presents with any signs and liaise with the hospital specialist where necessary. To report adverse events to the specialist and where appropriate the Commission on Human Medicines/MHRA (Yellow card scheme).

Monitoring parameter	**Recommended action if results not in normal range**
LFT's	• If deranged but not greater than 2 x upper limit, monitor. Refer back to Haematologist if not resolving. • If more than 2 x upper limit refer straight back to Haematologist.
U&E's	• If GFR 30-50mls/min, reduce dose to 1200mg daily, continue to monitor and inform Haematologist. • If GFR 10-30mls/min, reduce dose to 800mg daily, continue to monitor and inform Haematologist. • If GFR less than 10mls/min, stop treatment and refer back to Haematologist.
Calcium levels	• If low, stop treatment and refer back to Haematologist. • If high, inform Haematologist
Phosphate levels	• If deranged, contact Haematologist for advice.

Clinical Particulars

BNF therapeutic class	Section 6.4; Bisphosphonates
Contraindications and Cautions	Cautions: • Maintain adequate fluid intake during treatment • Atypical femoral fractures • Elderly – prescription potentially inappropriate (STOPP criteria) in patients with a current or recurrent history of upper gastrointestinal disease or bleeding Contraindications: • acute gastro-intestinal inflammatory conditions • pregnancy and breastfeeding • patients with severe renal failure where creatinine clearance is below 10ml/min • hypersensitivity to the active substance or to any of the excipients • patients receiving concomitant treatment with other bisphosphonates.
Adverse Drug Reactions	Common or very common • Bronchospasm • Nausea and vomiting (usually mild) • Diarrhoea (usually mild) • Skin reactions (hypersensitivity) • Asymptomatic hypocalcaemia • Influenza like illness • Oesophageal ulcer or oesophagitis (discontinue) Rare • Atypical femoral fractures Uncommon • Osteonecrosis of the jaw
Interactions	• Concomitant use of other bisphosphonates is contraindicated. • Patients receiving NSAIDs in addition to sodium clodronate have developed renal dysfunction. However, a synergistic action has not been established. • As aminoglycosides can cause hypocalcaemia concomitant clodronate should be administered with caution.

	• Concomitant use of estramustine phosphate with clodronate has been reported to increase the serum concentration of estramustine phosphate by 80% at the maximum. • Sodium clodronate forms complexes with divalent metal ions, and therefore simultaneous administration with food, antacids and mineral supplements may impair absorption.

Communication

Specialist to GP
The specialist will inform the GP when they have initiated Sodium Clodronate. When the patient is near completing the satisfactory initiation period, the specialist will write to the GP to request they take over prescribing and where possible give an indication as to the expected length of treatment. The Specialist will also send a Shared care request form to support the GP in undertaking reduced shared care. (Appendix A)

GP to specialist
If the GP has concerns over the prescribing of Sodium Clodronate, they will contact the specialist as soon as possible.

Contact names and details

Contact Details	Telephone number	Email
Consultant Haematologists: Dr D. Chan-Lam Youssef Sorour Robert Cutting Rumana Rashid	 01226 432810 01226 730000 01226 730000 01226 730000	 dchanlam@nhs.net y.sorour@nhs.net rcutting@nhs.net rumana.rashid@nhs.net
Haemato-Oncology Support Sister: Emma Sedgwick	01226 730000	emma.sedgwick1@nhs.net
Medicines Information: Gillian Turrell	01226 432857	gilliansmith2@nhs.net or medicinesinformation@nhs.net

References

1. BNF September 2015 Available at www.medicinescomplete.com
2. SPC Bonefos® Bayer Available at www.medicines.org.uk/emc/medicine/309
3. BCSH and UKMF Guidelines on the Management and Diagnosis of Multiple Myeloma Sept 2010. Available at www.bcsh**guidelines**.com/.../**MYELOMA**_Mngmt_**GUIDELINE**_REVISION_Sept_2010.pdf

Development Process
This guidance has been produced by Claire Johnston, Senior Pharmacist-Chemotherapy following an AMBER classification status of Sodium Clodronate by the Area Prescribing Committee. This guideline has been updated by Lauren Clarke in October 2020. This guideline has been subject to consultation and endorsement by the Area Prescribing Committee on 11th November 2020.

Appendix A – Shared Care request form (Amber)

- Specialist to complete when requesting GP to enter a shared care arrangement.
- GP to return signed copy of form.
- Both parties should retain a signed copy of the form in the patient's record.

From (**Specialist**): _____ **To** (**GP**): _____

Patient Details

Name: _____ ID Number: _____

Address: _____ DOB: _____

_____

Diagnosed condition: **Multiple Myeloma**

Amber Drug details

Drug name: **Sodium Clodronate** Dose: _____

Date of initiation: _____ Length of Treatment: _____

The patient will be reviewed by the Consultant on: _____

The patient should be reviewed by the GP by: _____

Monitoring

The following baseline tests have been carried out:

Parameter		BHNFT Reference Range	Result	Date test done
LFT's	Bilirubin	<21 micromol/L		
	ALT	0 – 40 units/L		
	AST	0 – 40 units/L		
	GGT	0 – 33 units/L		
	ALP	30 – 130 units/L		
U&E's	Sodium	133 – 146 mmol/L		
	Potassium	3.5 – 5.3 mmol/L		
	Creatinine	51 – 96 micromol/L		
	Urea	2.5 – 7.8 mmol/L		
Adjusted Calcium		2.1 – 2.6 mmol/L		
Serum Phosphate		0/8 – 1.5 mmol/L		

The following monitoring should be undertaken by the GP:

Parameter	Date next test due	Frequency
U&E's		Please indicate
LFT's		Please indicate
Adjusted Calcium		Please indicate
Serum Phosphate		Please indicate

Communication

Consultant
Telephone number: _____ Fax number:_____

Email address: _____

Specialist Nurse
Telephone number: _____ Fax number: _____

Email address: _____

Confirmation of acceptance of shared care

Specialist (Doctor/Nurse) name: _____

Specialist (Doctor/Nurse) signature: _____ Date: _____

I, Dr …….., can confirm I :

☐ accept the request to participate in shared care for the patient named above.

☐ reject the request to participate in shared care for the patient named above. The reason for this being ……..

GP signature: _____ Date: _____

To save resources you have been sent appendix A of the shared care document. The full document (Sodium Clodronate (Bonefos) Shared Care Guideline for the treatment and prevention of bone disease in multiple myeloma, date approved November 2020) can be accessed on the Barnsley BEST website at the following link:
http://best.barnsleyccg.nhs.uk/clinical-support/medicines/shared-care-guidelines/

Or via the Barnsley Area Formulary www.barnsleyformulary.nhs.uk