Ibandronic acid (Amber with shared care)

Shared Care Guidelines: For the treatment of adjuvant therapy for postmenopausal patients with early breast cancer **'off label'** use. Bisphosphonates have been shown to reduce the rate of breast cancer recurrence in the bone and improve breast cancer survival; definite benefit has been demonstrated only in postmenopausal women.

AREAS OF RESPONSIBILITY FOR THE SHARING OF CARE

This shared care agreement outlines suggested ways in which the responsibilities for managing the prescribing of medicine name and indication shared between the specialist and general practitioner (GP). GPs are **invited** to participate. If the GP is not confident to undertake these roles, then he or she is under no obligation to do so. In such an event, the total clinical responsibility for the patient for the diagnosed condition remains with the specialist. If a specialist asks the GP to prescribe this drug, the GP should reply to this request as soon as practicable.

Sharing of care assumes communication between the specialist, GP and patient. The intention to share care is usually explained to the patient by the doctor initiating treatment. It is important that patients are consulted about treatment and are in agreement with it. Patients with the condition are under regular specialist follow-up, which provides an opportunity to discuss drug therapy.

The doctor who prescribes the medication legally assumes clinical responsibility for the drug and the consequences of its use.

RESPONSIBILITIES and ROLES

	Specialist responsibilities
1	Initiate ibandronate 50mg daily and provide 3 months supply
2	Discuss the rationale for treatment benefits and side effects of treatment with the patient including details relating to osteonecrosis of the jaw (MHRA), atypical fractures of the femur (MHRA), oesophageal reactions (MHRA), Very rare reports of osteonecrosis of the external auditory canal (MHRA warning)
3	Ensure the patient has received a PIL and is aware of the 'off licence' use of ibandronate (approved by the Trust DTC)
4	Perform baseline blood tests including FBC, U&E LFT, renal function and serum calcium and phosphates. Baseline DEXA is NOT required. Repeat blood tests 2-3 months after starting ibandronic acid.
5	Adequate intake of calcium and vitamin D is important in all patients: All patients should be advised to take supplemental vitamin D 20-25 micrograms (800-1000 IU) daily, which may be bought over the counter (OTC) from pharmacies, supermarkets or health food shops or prescribed by the GP. If dietary intake of calcium is low, prescribe a combined calcium and vitamin D preparation. Include in GP letter whether calcium and vitamin D needs to be prescribed or patient has been advised to buy vitamin D
6	Instruct patient on how to take oral ibandronic acid safely and reliably (fasting, early morning, upright, swallowed whole with at least 200ml of water etc.). Ensure patient can follow administration recommendations
7	Review current medicines: Advise patient to stop any other bisphosphonate that they may be taking; for example: risedronate or alendronate. For patients taking a regular NSAID consider whether this can be discontinued. Occasional use of a mild NSAID such as ibuprofen is acceptable.
8	Ask the GP whether he or she is willing to participate in shared care, and agree with the GP as to who will discuss the shared care arrangement with the patient
9	Review the patient's condition and monitor response to treatment regularly where indicated.
10	Give advice to the GP on when to stop treatment (up to 3 years)
11	Report adverse events to the MHRA
12	Ensure that clear backup arrangements exist for GPs to obtain advice and support.

	General Practitioner responsibilities
1	Reply to the request for shared care as soon as practicable.
2	Prescribe medicine at the dose recommended. Issue on-going prescriptions for ibandronic acid 50mg daily for length of time specified by hospital specialist (consider adding stop date to dosing instructions).
3	Ensure other bisphosphonates are stopped during this period.
4	Refer promptly to specialist when any loss of clinical efficacy is suspected (e.g. worsening of disease-related symptoms, new symptoms suggestive of disease recurrence or progression) or intolerance to therapy occurs.
5	Report to and seek advice from the specialist on any aspect of patient care that is of concern to the GP and may affect treatment.
6	Undertake annual medicine review including blood tests FBC U&E LFT Calcium and Phosphate levels
7	Stop treatment on the advice of the specialist.
8	Report adverse events to the specialist and MHRA.

Patient's role	
1	Report to the specialist or GP if she does not have a clear understanding of the treatment.
2	Share any concerns in relation to treatment with medicine.
3	Report any adverse effects to the specialist or GP whilst taking the medicine

BACK-UP ADVICE AND SUPPORT

Contact details	Telephone No.	Email address:
Specialist: Dr Mark Beresford Consultant Medical Oncologist	Via secretary	mark.beresford@nhs.net
Specialist: Dr Rebecca Bowen Consultant Medical Oncologist	Via secretary	rebecca.bowen3@nhs.net
Hospital Pharmacy Dept: Vicki Portingale Sarah Murdoch Oncology Pharmacists	Tel: 01225 428331 Ext 1726	vicki.portingale@nhs.net sarahmurdoch@nhs.net
Other:		

SUPPORTING INFORMATION

Bisphosphonates reduce the rate of bone turnover. Bisphosphonates may be used in some people with breast cancer, within the terms of their licenses, to prevent and treat osteoporosis or skeletal events, or manage osteolytic lesions, bone pain or hypercalcaemia of malignancy. However, these treatments are not licensed for preventing recurrence or improving survival in people with early breast cancer, and use for this indication is **off-label.**

Treatment Aims (Therapeutic plan)
A large collaborative meta-analysis (involving 18,766 women of whom 11,767 were post-menopausal) found that for post-menopausal women with breast cancer adjuvant bisphosphonates reduced the rate of breast cancer recurrence and improved breast cancer survival.

The absolute reduction with bisphosphonate use in post-menopausal women at 10 years was 3.0% for breast cancer recurrence (from 25.8%); 3.4% for distant recurrence (from 21.2%); 2.2% for bone recurrence (from 8.8%); and 3.3% for breast cancer mortality (from 18.0%).

This benefit was only seen with certain bisphosphonates including zoledronic acid IV 6 monthly and oral ibandronic acid 50mg daily.

There is clinical support for the introduction of bisphosphonates for this cohort of women. It is included in the NHS England breast cancer CRG service specification and endorsed as a priority for implementation at the UK Breast Cancer Meeting (UKBCM) in November 2015.

Treatment Schedule (including dosage and administration)
The hospital specialist will arrange the first prescription for ibandronic acid 50mg daily and will request on-going prescribing by the GP. The specialist will specify the length of treatment (up to 3 years).

Contra-indications and precautions for use
Contraindications
- Hypersensitivity to ibandronic acid or any excipients in tablets.
- Abnormalities of the oesophagus which delay oesophageal emptying such as stricture or achalasia.
- Inability to stand or sit upright for at least 60 minutes
- Pregnancy

Cautions

Patients with renal impairment

- No dose adjustment is necessary for patients with mild renal impairment (CrCl greater than or equal to 50 and less than 80 mL/min)
- For patients with moderate renal impairment (CrCl greater than or equal to 30 and less than 50 mL/min) a dose adjustment to one 50mg tablet every second day is recommended
- For patients with severe renal impairment (CrCl less than 30 mL/min) a dose adjustment to one 50mg tablet once weekly is recommended

Creatinine clearance (CrCl) in this document may be approximated to eGFR in primary care for patients with a BMI between 18.5 and 30kg/m^2. The values remain the same but the units become mL/min/1.73m

Osteonecrosis of the jaw

Avoid invasive dental procedures while on bisphosphonate treatment. If invasive dental procedures are unavoidable then stop bisphosphonate for at least 6 weeks prior to the procedure. Treatment can normally resume once bone socket healing has fully occurred. Seek specialist advice if unsure.

Atypical fractures of the femur

Atypical femoral fractures have been reported in patients receiving bisphosphonates. Atypical femoral fractures may occur with little or no trauma in the sub-trochanteric and diaphyseal regions of the femur. Atypical femoral fractures have also been reported in patients with certain comorbid conditions (e.g. vitamin D deficiency, rheumatoid arthritis, hypophosphatasia) and with use of certain pharmaceutical agents (e.g. bisphosphonates, glucocorticoids, proton pump inhibitors). These events have also occurred without antiresorptive therapy. Similar fractures reported in association with bisphosphonates are often bilateral; therefore the contralateral femur should be examined in bisphosphonate-treated patients who have sustained a femoral shaft fracture. Discontinuation of bisphosphonate therapy in patients suspected to have an atypical femur fracture should be considered pending evaluation of the patient based on an individual benefit-risk assessment. During bisphosphonate treatment, patients should be advised to report new or unusual thigh, hip, or groin pain. Patients presenting with such symptoms should be evaluated for an incomplete femoral fracture.

Side-effects

Full list of side effects / contraindications is given in the ibandronic acid 50mg tablets SPC (Summary of Product Characteristics) available from https://www.medicines.org.uk/emc/product/4642/smpc

Special warnings and precautions for use:

- The risk of severe oesophageal adverse experiences appears to be greater in patients who do not comply with the dosing instructions.
- Use with caution in patients with active or recent upper gastrointestinal problems
- MHRA/CHM advice: Bisphosphonates use and safety (December 2014)
- MHRA/CHM advice: Bisphosphonates: atypical femoral fractures (June 2011)
- MHRA/CHM advice: Bisphosphonates: osteonecrosis of the jaw (November 2009)
- MHRA/CHM advice: Bisphosphonates: very rare reports of osteonecrosis of the external auditory canal (December 2015)

Monitoring

Parameter	Frequency of monitoring	Action (adjustment and referral back to hospital)
Renal function	Annual	If calcium is out-of-range or renal impairment becomes severe (eGFR less than 30ml/min/1.73m2) discontinue ibandronic acid and contact hospital specialist for advice. Reduce dose if eGFR less than 50ml/min/1.73m2 (see page x for information on dosing in patients with renal impairment)
Serum Calcium	Annual	

Drug Interactions

Full list of interactions is given in the ibandronic acid 50mg tablets SPC
https://www.medicines.org.uk/emc/product/4642/smpc
Absorption of bisphosphonates is reduced when administered concurrently with antacids or oral iron (see BNF). Drug – food interactions occur. Products containing calcium and iron including milk and food are likely to interfere with the absorption of Ibandronic acid tablets.
Caution is advised when administered with aminoglycosides or NSAIDs

Information for patients

- Patients need to be aware that this is an unlicensed indication (responsibility of specialist). See Appendix 2.
- Patients should be advised on how to take the medicines and be referred to the manufacturer's patient information leaflet for full details. In addition a specific leaflet has been produced to support this use – See Appendix 2.
- Patients and carers should be advised to stop tablets and seek medical attention for symptoms of oesophageal irritation such as dysphagia, pain on swallowing, retrosternal pain, or heartburn.
- During treatment patients should maintain good oral hygiene, receive routine dental check-ups, and report any oral symptoms such as dental mobility, pain or swelling, non-healing sores or discharge to a doctor and dentist.
- Patients should be advised to report any ear pain, discharge from the ear or an ear infection during treatment with a bisphosphonate.
- Patients should be advised to report any thigh, hip or groin pain during treatment with a bisphosphonate.
- Patients should be advised to contact their GP if they have any concerns with the medication.

Cost

At current prices, one year's treatment with ibandronate 50mg daily is £8

References

There is no NICE guidance but NICE has published a Medicines Evidence Summary Early breast cancer (preventing recurrence and improving survival): adjuvant bisphosphonates ES15 July 2017
https://www.nice.org.uk/advice/es15/chapter/Key-points

1. Early Breast Cancer Trialists' Collaborative Group (2015). Adjuvant bisphosphonates treatment in early breast cancer: meta-analyses of individual patient data from randomised trials. Lancet 386:1353-61. http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(15)60908-4/abstract
2. Adjuvant bisphosphonates in early breast cancer: consensus guidance for clinical practice from a European Panel (2016), Annals of Oncology 27:379-390. http://annoc.oxfordjournals.org/content/27/3/379.full.pdf+html.
3. UK Breast Cancer Meeting (UKBCM). November 2015. Presentations available here: http://www.ukbcg.org/content.php?id=245g=6/Presentations-2015.
4. Summary of Product Characteristics. Ibandronic Acid 50mg tablets. www.medicines.org.uk.
5. BNF April 2018 https://bnf.nice.org.uk/drug/ibandronic-acid.html .
6. NICE Medicines Evidence Commentary, November 2015, Early breast cancer: adjuvant bisphosphonate treatment beneficial in post-menopausal women. http://www.medicinesresources.nhs.uk/GetDocument.aspx?pageId=802403.
7. Prescribing Guidance for Ibandronic Acid 50mg tablets in post-menopausal women with breast cancer. The Sheffield Prescribing Group. July 2016.

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Document details

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