NHS
Kent and Medway
Cancer Collaborative

Bisphosphonate Guidelines

For early breast cancer (zoledronic acid) and the prevention of skeletal related events.

Network Guidance Document

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1.0 GUIDELINES FOR DENTAL PROCEDURES AND PATIENTS PRESENTING WITH EAR SYMPTOMS, OR THIGH, HIP OR GROIN PAIN

- A dental examination with appropriate preventive dentistry and an individual benefit-risk assessment is recommended prior to treatment with bisphosphonates.
- Do not start treatment in patients with an active dental or jaw condition requiring surgery or in patients who have not completely recovered following oral surgery.
- A minimum of 4 weeks should have passed before starting treatment following dental procedures where bone has been exposed or manipulated.
- While on treatment avoid dental procedures if possible.
- Patients should be encouraged to have regular dental check-ups whilst on treatment, at least every 6 months.
- If patients require **invasive** dental procedures (i.e.: dental extraction, surgical dental extraction or root planing /deep scaling) then the patient is required, where possible, to stop treatment 8 weeks prior, and recommence treatment when there is mucosal healing as assessed by a dental professional (there is no need to wait 8 weeks post procedure if full mucosalisation has occurred). N.B.: Superficial dental fillings (drilling), normal hygiene appointments, the provision of dentures and routine root canal therapy are not invasive dental procedures and therefore there is no indication to stop bisphosphonate therapy for these.
- Patients who develop osteonecrosis of the jaw should be referred to a maxillofacial surgeon.
- Caution is advised when zoledronic acid is administered with anti-angiogenic drugs (e.g. bevacizumab, sunitinib, pazopanib), as an increase in the incidence of ONJ has been observed in patients treated concomitantly with these medicinal products.
- Reference should be made to the UK chemotherapy board guidance on medication related osteonecrosis of the jaw:
  - https://www.uksactboard.org/medication-related-osteonecrosis-of-the-jaw-guidance-for-the-oncology-multi-disciplinary-team
- The possibility of osteonecrosis of the external auditory canal should be considered in patients receiving bisphosphonates who present with ear symptoms including chronic ear infections.
- During bisphosphonate treatment patients should be advised to report any thigh, hip or groin pain and any patient presenting with such symptoms should be evaluated for an incomplete femur fracture.

NB Dental assessment by dentist is not mandatory when bisphosphonates are used for the urgent treatment of hypercalcaemia (see separate hypercalcaemia guidelines)

2.0 PRIOR TO STARTING BISPHOSPHONATE

1. **Renal function (including corrected calcium, phosphate and magnesium), liver function and bone profile MUST be reviewed at baseline and prior to the administration of EACH dose of bisphosphonate.**

NB: For calculation of creatinine clearance refer to the KOC intranet Cockcroft & Gault calculator.

2. **Normal reference ranges**

Trust	**Corrected calcium** mmol/l	**Serum creatinine** umol/l	**Urea** mmol/l	**Phosphate** mmol/l	**Magnesium** mmol/l
MTW	2.2 – 2.6	44 – 80 female 62-106 male	2.5 – 7.8	0.8 – 1.5	0.7 – 1.0
Medway	2.0 – 2.60	45-84	2.5-7.8	0.8 – 1.51	0.7 – 1.0
East Kent	2.2 – 2.6	64-104	2.5 – 7.8	0.8 – 1.5	0.7 – 1.0
Dartford & Gravesham	2.2 – 2.6	45 – 84	2.5 – 7.8	0.8 – 1.5	0.7 – 1.0

3. **Prescribe initial bisphosphonate dose based on baseline creatinine clearance.**

Baseline creatinine clearance (ml/min)	**Zoledronic Acid dose**	**Pamidronate dose**	**Oral Ibandronic acid** Dose / frequency
>60	4.0mg	90mg	50mg / daily
50 - 60	3.5mg	90mg	50mg / daily
40 - 49	3.3mg	90mg	50mg on alternate days
30 - 39	3.0mg	90mg	50mg on alternate days
< 30	Not recommended as per SPC - consider Ibandronic Acid	Discuss with consultant. Reduce rate of administration to 20mg/hr in impaired renal function. (90mg / 270 mins)	50mg / weekly

3.0 DURING TREATMENT

4. **Review serum creatinine (SrCr) prior to each dose.**

Zoledronic acid and Pamidronate

Baseline serum creatinine	WITHHOLD TREATMENT IF CREATININE INCREASES BY	INFORM CONSULTANT IF CREATININE INCREASES BY
<124µmol/L	44µmol/L	44µmol/L
≥124µmol/L	88µmol/L	44µmol/L

- Following a dose delay, repeat bloods after 4 weeks and recommence when SrCr is below or within + 10% of baseline.
- If ibandronic acid is used, discuss any significant rise in serum creatinine with consultant; deterioration of renal function on long term ibandronic acid was not noted in clinical trials.

3.1 Prevention of Hypocalcaemia

Calcium 600mg + colecalciferol 10 micrograms (Adcal D3) once a day should be given to prevent hypocalcaemia with zoledronic acid.

3.2 Management of Hypocalcaemia, Hypomagnesaemia and Hypophosphataemia

Patients with corrected serum calcium below the normal reference range should be discussed with the consultant, to consider extra calcium supplementation. Hypocalcaemia is usually asymptomatic and does not require IV treatment, but ensure that the patient is taking daily calcium and vitamin D supplements. Serum magnesium should also be checked in these patients to determine whether magnesium replacement is required.

The decision whether to continue or defer the dose of zoledronic acid may depend upon the degree and duration of hypocalcaemia, as well as clinician preference and clinical situation.

Short-term supplemental therapy (IV or oral) may be advised to correct hypophosphataemia while bisphosphonate treatment continues.

NB refer to individual trust policy for further guidance on electrolyte replacement.

4.0 REFERENCES

- Zometa© Zoledronic Acid (accessed online 16/12/2021) Summary of Product Characteristics
- Pamidronate (accessed online 16/12/2021) Summary of Product Characteristics
- ZICE Protocol (Zoledronate versus Ibandronic acid Comparative Evaluation) (07/2007)
- Bondronat© Ibandronic acid Oral (accessed online 16/12/2021) Summary of Product Characteristics.

5.0 DOCUMENT ADMINISTRATION

Document Title	Bisphosphonate guidelines incorporating prescribing in renal impairment
Principal author	C.Waters
Co-author(s)	KMCC chemotherapy Group
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The document is located http://www.kmcc.nhs.uk/medicines-and-prescribing-incorporating-sact-pathways/sact-pathways-guidelines-for-the-management-of-sact-induced-adverse-reactions-and-nursing/	
KMCC document: No responsibility will be accepted for the accuracy of this information when used elsewhere.	
Enquiries:	Caroline Waters. Lead Oncology Pharmacist, Kent and Medway Cancer Collaborative
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Revision History			
Date of revision	New Version Number	Nature of Revision	Confirmation of Accuracy by
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June 2018	2	Published following consultation with KMCC Chemotherapy Groups (circulated via email)	
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January 2022	2.2	Updated by M.Archer/C.Waters following trust review	Circulated for comment.
January 2022	2.3	Update to Renal function parameters section 2.0	Parameters updated by Marcher: parameters sent by lead pharmacists for each trust via email

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