Clinical Guideline

MALIGNANT HYPERCALCAEMIA IN ADULTS

SETTING Trust-wide

FOR STAFF Medical Staff, Pharmacy Staff, Nursing Staff

PATIENTS Adult patients with confirmed malignant hypercalcaemia (patients with known malignancy and a serum corrected calcium >2.8mmol/L)

Key Background

Symptoms of hypercalcaemia are unpleasant and reversible, so for most patients, treatment will be appropriate. However, for some patients, e.g. those in the last few days of life, it may not be appropriate to carry out repeated blood tests or to treat the hypercalcaemia. Assessment of each patient as an individual is needed in order to ensure they are treated appropriately.

Clinical Symptoms

- Fatigue/Lethargy
- Anorexia/Nausea/Vomiting
- Abdominal Pain/Constipation
- Polyuria/Thirst
- Hypertension/Cardiomyopathy/QT Changes/Dysrhythmias
- Muscle Weakness
- Confusion/Seizures/Coma

Guidance

- Investigations include serum calcium, albumin, U+E's, phosphate, Vitamin D, ECG, Corrected Calcium (Serum Ca + 0.02 x (40 - Serum Albumin))
- Consider checking serum parathyroid hormone if patient has no known bone metastases
- If patient is already taking oral bisphosphonate, hypercalcaemia still needs to be treated
- Review and aim to stop medication that can potentiate hypercalcaemia, e.g. thiazide diuretics, lithium carbonate, calcium supplements, calcium-containing antacids, colecalciferol, retinoids (If unsure, consult pharmacist or summary of product characteristics[1])
- If the patient has renal impairment, review medicines which may affect renal blood flow e.g. non-steroidal anti-inflammatories, diuretics, angiotensin receptor blockers, ACE inhibitors.

If serum corrected calcium is 2.80 – 3.00 mmol/L **without** symptoms:

1. Encourage patient to drink plenty or rehydrate with intravenous (IV) sodium chloride 0.9%
2. Review medications as above
3. Plan to recheck serum corrected calcium within a week

If serum corrected calcium is 2.80 – 3.00 mmol/L **with** symptoms or if serum corrected calcium >3.00mmol/L:

1. All patients should be rehydrated before having bisphosphonate: unless contraindicated, administer 2-4 litres IV sodium chloride 0.9% over 24 hours (+/- potassium supplements if indicated). Ensure adequate urine output (>100-150ml/h).
2. Review medications as above.
3. Give IV bisphosphonate (drug and dose dependent upon renal function).

Creatinine Clearance (ml/min)	Dose	Diluent and Duration
>60	4mg Zoledronic Acid	100ml sodium chloride 0.9% over 15 minutes.
50-60	3.5mg Zoledronic Acid	
40-50	3.3mg Zoledronic Acid	
30-40	3.0mg Zoledronic Acid	
<30	2mg Ibandronic Acid	500ml Sodium Chloride 0.9% over 2 hours[2].

4. Recheck renal function, phosphate and magnesium 24 hours after treatment.
5. Recheck serum corrected calcium after bisphosphonate (4-7 days after or sooner if monitoring fluid replacement).
6. If the patient becomes profoundly hypocalcaemic, short term calcium supplements may be indicated.
7. If serum corrected calcium remains elevated 5-7 days post treatment: repeat dose (unlicensed) after consultation with oncologist/endocrinology team. Consider maximum effect may not yet have been achieved and repeat dosing may cause hypocalcaemia. Do not give further dose until at least four days after previous dose.
8. If resistant hypercalcaemia, not responding to initial treatment, please consult with patients consultant or endocrinologist for consideration of further treatment including options such as denosumab[3].
9. Consider calcitonin (4IU/kg sc bd, can be increased to 8IU/kg tds) if rapid control of calcium is required, or in patients with bisphosphonate/denosumab resistant hypercalcaemia. The effect of calcitonin is usually short-lived, in the region of 48 hours, even with repeated administrations beyond that time frame[6].
10. In some patients, dialysis may be appropriate.
11. Plan to recheck serum corrected calcium after three weeks or earlier if symptoms return.

Table A

REFERENCES	1. Summary of Product Characteristics: Zoledronic acid 4mg/100ml concentrate for solution for infusion, last updated 11/03/2019 [Accessed online on 17/04/2020]. https://www.medicines.org.uk/emc/product/5298/smpc 2. Summary of Product Characteristics: Bondronat 2mg concentrate for solution for infusion, last updated 20/05/2019 [Accessed online on 19/04/2020]. https://www.medicines.org.uk/emc/product/9374/smpc 3. Xgeva (Denosumab) injection for subcutaneous use. Initial U.S. approval: 2010. Revised 02/2020. [Accessed online on 17/04/2020]. http://pi.amgen.com/united_states/xgeva/xgeva_pi.pdf 4. Walsh J, Gittoes N, Selby P. Society for endocrinology endocrine emergency guidance. Emergency management of acute hypercalcaemia in adult patients. Sept 2016. [Accessed online 17/04/2020] https://ec.bioscientifica.com/view/journals/ec/5/5/G9.xml 5. Acute Oncology Initial Management Guidelines. Version 2. Reviewed 01/03/2020 [Accessed online 17/04/2020] https://www.ukons.org/site/assets/files/1134/acute_oncology_initial_management_guidelines.pdf 6. Shane E, Berenson J. Treatment of hypercalcaemia. Updated Feb 2020. link [Accessed Online 28/04/2020]
RELATED DOCUMENTS AND PAGES	N/A
AUTHORISING BODY	BHOC Clinical Governance Group
SAFETY	All bone-modifying agents (Denosumab, Zoledronic acid, Ibandronic acid) are recognised to cause osteonecrosis of the jaw as a side-effect.
QUERIES AND CONTACT	*For oncology advice:* • 09:00 – 17:00 Oncology registrar via bleep [redacted] • Out of Hours: Oncology via switchboard *For palliative care advice:* • 09:00 – 17:00 Palliative Care Team via x[redacted] • Out of Hours: Oncology via switchboard For endocrinology advice: 09:00-17:00 Endocrine registrar via bleep [redacted]

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