**Title of Guideline:** Management of Hypercalcaemia of Malignancy

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**Division & Specialty:** Medicine / Specialist Services

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**Guideline Number:** CG13-022

**Version Number:** 2

**Date of Review:** November 2017

**Explicit definition of patient group to which it applies:** Adult patients with malignancy and hypercalcaemia within WWL.

**Abstract**

**Statement of evidence base of the guideline**

<table>
<thead>
<tr>
<th>Evidence Base (1-5)</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1a</td>
<td>Meta analysis of RCT</td>
</tr>
<tr>
<td>1b</td>
<td>At least 1 RCT</td>
</tr>
<tr>
<td>2a</td>
<td>At least 1 well designed controlled study without randomisation</td>
</tr>
<tr>
<td>2b</td>
<td>At least 1 other well designed quasi experimental study</td>
</tr>
<tr>
<td>3</td>
<td>Well –designed non-experimental descriptive studies (i.e. comparative / correlation and case studies)</td>
</tr>
<tr>
<td>4</td>
<td>Expert committee reports or opinions and / or clinical experiences of respected authorities</td>
</tr>
<tr>
<td>5</td>
<td>Recommended best practise based on the clinical experience of the guideline developer</td>
</tr>
</tbody>
</table>

**Consultation Process**

**Target Audience**

*This guideline has been registered with the Trust. However, clinical guidelines are guidelines only. The interpretation and application of clinical guidelines will remain the responsibility of the individual clinician. If in doubt contact a senior colleague or expert. Caution is advised when using guidelines after the review date.*
1.0 Definition of Hypercalcaemia

1.1 Hypercalcaemia is defined as an adjusted serum calcium >2.60 mmol/l.

1.2 Treatment may not be required in mild hypercalcaemia (serum calcium 2.60 – 2.99mmol/l.) if the patient is asymptomatic.

1.3 Treatment is required if the patient is symptomatic and/or serum calcium is ≥ 3.0mmol/l.

1.4 Adjusted calcium >4 mmol/l is life-threatening & requires URGENT treatment.

2.0 Scope of the guideline

2.1 This guideline refers to the management of hypercalcaemia due to malignancy.

2.2 If patient has hypercalcaemia and metastatic cancer, initiate treatment as per this guideline and refer patient to Acute Oncology or Palliative Care Team.

2.3 If patient has hypercalcaemia and is not known to have cancer, or they have cancer but it is not known to be metastatic, seek advice from Endocrinologist regarding investigation and management.

3.0 Symptoms of hypercalcaemia

3.1 Typical acute presentations of symptomatic hypercalcaemia usually include

- nausea and vomiting
- thirst and polydipsia
- polyuria
- clinical dehydration
- agitation and confusion
- palpitations (atrial and ventricular arrhythmias, bradycardia)

3.2 More subtle symptoms include anorexia, abdominal pain, constipation, bone pain, lethargy and muscle weakness.

4.0 Management of Hypercalcaemia (see flow chart – Appendix 1)

4.1 Assess patient’s clinical condition (are they symptomatic?) and determine if treatment is appropriate and in line with their wishes.

4.2 Check U&E, eGFR, PTH, phosphate and magnesium if not already done.

4.3 Review medication. Stop calcium supplements and consider stopping any drugs which may affect renal blood flow and calcium levels e.g. thiazide diuretics. Refer to AKI guidelines as appropriate http://intranet.xwwl.nhs.uk/Departments/AKI/default.asp .
4.4 Pre-hydrate the patient with 3 litres of 0.9% Sodium Chloride intravenously over 24 hours, unless there are risk factors for fluid overload (e.g. renal impairment or cardiac problems), or patient is on fluid restriction. Adjust rate and volume of fluids according to age, severity of hypercalcaemia and degree of dehydration. In cases of renal or cardiovascular compromise, seek senior advice from either an SpR or Consultant to determine an appropriate intravenous rehydration regime.

4.5 Following rehydration, give zoledronic acid according to chart in section 5. If eGFR < 30, DO NOT GIVE BISPHOSPHONATE, SEEK ADVICE* from Acute Oncology or Palliative Care Team.

4.6 Recheck U&E & calcium levels after 5 - 7 days, or as clinically indicated to monitor condition and determine need for further fluid replacement. Note - serum calcium usually takes 3-5 days to fall and 7-10 days to achieve maximal effect following zoledronic acid.

4.7 If serum calcium level remains elevated at 7 days and symptoms not improving, seek specialist advice from Acute Oncology or Palliative Care Team. Bisphosphonates should not normally be given again within 3 weeks, as there is a risk of hypocalcaemia if given too soon.

4.8 Monitor calcium levels weekly as long as risk of hypercalcaemia remains or more frequently if symptoms dictate.

5.0 Dosing and administration of zoledronic acid

5.1 Zoledronic acid should not be given to patients with severe renal failure i.e. eGFR <30, unless risk-benefit ratio has been considered carefully i.e. is the risk to life from hypercalcaemia so great that the benefit of treatment would outweigh the risk. SEEK ADVICE IF NECESSARY from Acute Oncology or Palliative Care Team.

5.2 Give Zoledronic Acid IV in 100ml of 0.9% Sodium Chloride over at least 15 minutes; dose dependant on renal function as table below

5.3 *Note caution is needed in the use of eGFR to interpret renal function in some patients; Cockcroft Gault calculation should be considered to determine creatinine clearance in frail elderly and cachectic patients (see Appendix 2)

5.4 Zoledronic acid dosing according to renal function

<table>
<thead>
<tr>
<th>e-GFR</th>
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<tbody>
<tr>
<td>&gt;60</td>
<td>4 milligrams</td>
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<tr>
<td>50 - 60</td>
<td>3.5 milligrams</td>
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<tr>
<td>40-49</td>
<td>3.3 milligrams</td>
</tr>
<tr>
<td>30-39</td>
<td>3 milligrams</td>
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5.5 Hypophosphataemia is a common side effect of bisphosphonates but may not need intervention. SEEK ADVICE FROM ACUTE ONCOLOGY TEAM OR PHARMACY IF NECESSARY.
6.0 References

Wigan Borough Palliative Care Pain & Symptom Control Guidelines – Version 2, July 2010
The Christie NHS Foundation Trust Acute Oncology Handbook – Version V8, November 2013


**Management of Hypercalcaemia of Malignancy**

- Hypercalcaemia is defined as an adjusted serum calcium > 2.60 mmol/l.
- If adjusted calcium is 2.60 – 2.99 mmol/l, treatment may not be required if patient asymptomatic.
- *Adjusted calcium > 4mmol/l. is life threatening & requires URGENT treatment and referral to Acute Oncology and/or Palliative Care.*

### Signs and Symptoms of Hypercalcaemia

- Polyuria
- Anorexia
- Constipation
- Fatigue
- Lethargy
- Arrhythmias
- Polydipsia
- Nausea/vomiting
- Abdominal pain
- Confusion
- Seizure
- Coma

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**If adjusted calcium > 2.60 mmol/l & not known to have metastatic cancer and/or PTH elevated or not suppressed**

**SEEK ENDOCRINOLOGY ADVICE**

**Monitor symptoms**

Recheck calcium + treat only if levels rising or patient develops symptoms

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**If calcium still high 7 days following initial bisphosphonate and symptoms not improving**

**SEEK ADVICE** from Acute Oncology or Palliative Care Team

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**Sources of Advice:**

- Acute Oncology - Ext 2710
- Palliative Care - Ext 2008
- Pharmacy - Ext 2466
- Endocrinologist - Ext 2188

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*Consider Cockcroft Gault formula in frail elderly and cachectic patients.*

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**Common side-effects of Bisphosphonates**

- Fever & flu-like illness
- Symptomatic hypocalcaemia
- Renal impairment
- Nausea & vomiting
- Hypophosphataemia
- Hypomagnesaemia

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For **FURTHER INFORMATION** see full guidance on intranet.
Cockcroft Gault Calculation

Creatinine clearance (CrCl ml/min): \[ N^* \times \frac{140 - \text{age (years)}}{\text{weight (kg)}} \times \text{serum creatinine (micromol/L)} \]

* \(N^* = 1.23\) for males, \(1.04\) for females

- calculations should be second checked as a matter of good practice
- contact Pharmacy for advice if necessary