

Title of Guideline	Management of Hypercalcaemia of Malignancy
Contact Name and Job Title (Authors)	Dr Jenny Wiseman - Consultant in Palliative Medicine Dr Aruna Hodgson - Consultant in Palliative Medicine Dr Denise Darby - Consultant Chemical Pathologist Dr Rahul Peck – Speciality Doctor in Medical Oncology Dr Daniel Kannappan - Consultant Endocrinologist Dr Elena Takeuchi – Consultant Medical Oncologist Barbara Hefferon – Acute Oncology Nurse Specialist Simon Langridge - Medicine Information Pharmacist Janette Sanders -Macmillan Palliative Care Nurse Specialist
Division & Specialty	Medicine / Specialist Services
Date of Submission	
Guideline Number	CG13-022
Version Number	2
Date of Review	
Approving Committee(s)	
Date of Approval	
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 Evidence Base (1-5)	Level 3
1a	Meta analysis of RCT
1b	At least 1 RCT
2a	At least 1 well designed controlled study without randomisation
2b	At least 1 other well designed quasi experimental study
3	Well –designed non-experimental descriptive studies (i.e. comparative / correlation and case studies)
4	Expert committee reports or opinions and / or clinical experiences of respected authorities
5	Recommended best practise based on the clinical experience of the guideline developer
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.	

Title of Guideline: Management of Hypercalcaemia of Malignancy

Date of Submission: November 2015

Date of Review: November 2017

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 $2.60 - 2.99$ mmol/l.) if the patient is asymptomatic.
- 1.3 Treatment is required if the patient is symptomatic and/or serum calcium is ≥ 3.0 mmol/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.xwww.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	
e-GFR	Dose
>60	4 milligrams
50 - 60	3.5 milligrams
40-49	3.3 milligrams
30-39	3 milligrams

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.

Title of Guideline: Management of Hypercalcaemia of Malignancy

Date of Submission: November 2015

Date of Review: November 2017

6.0 References

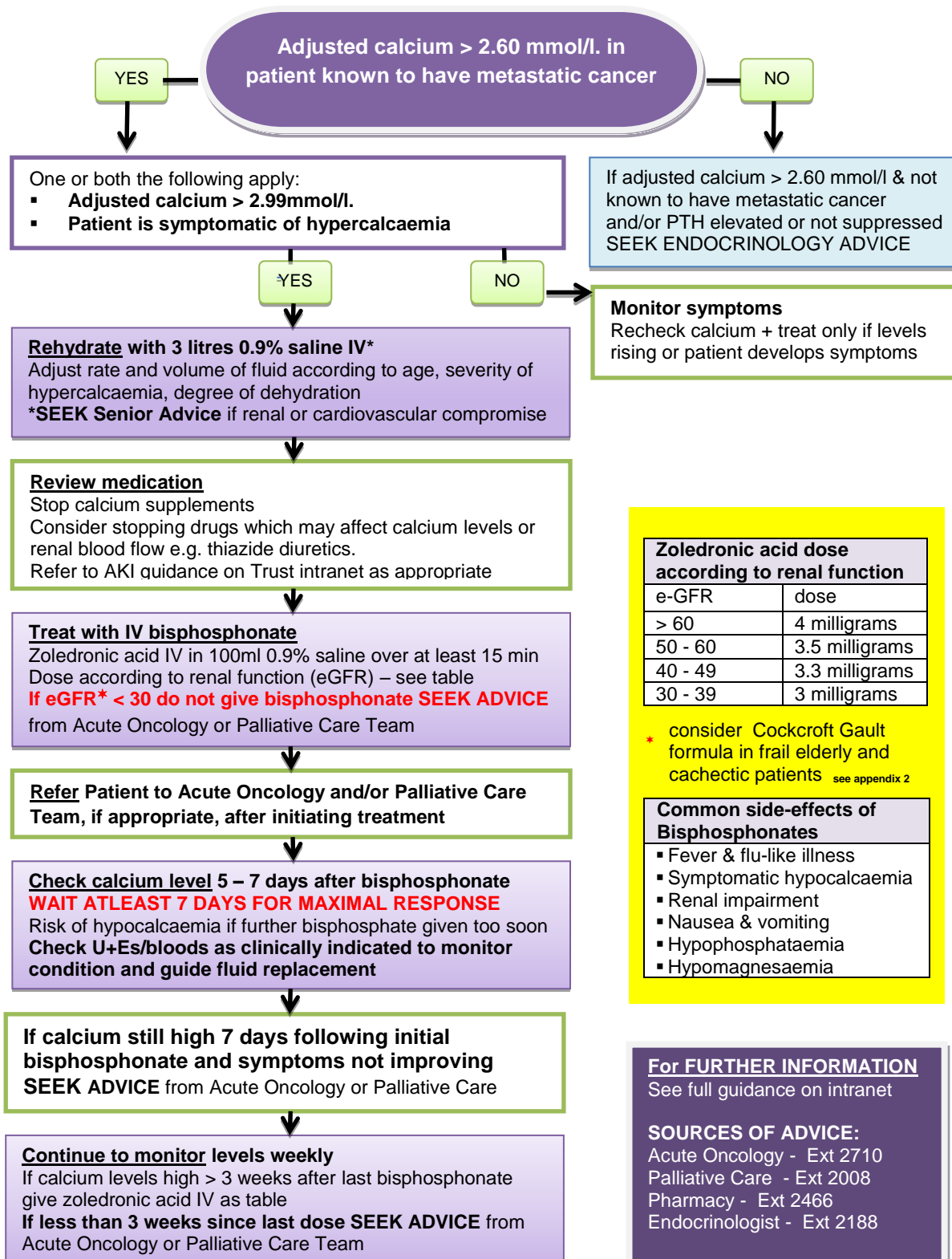
- Wigan Borough Palliative Care Pain & Symptom Control Guidelines – Version 2, July 2010
- The Christie NHS Foundation Trust Acute Oncology Handbook – Version V8, November 2013
- Twycross R, Wilcock A, Howard E (Eds) (2014) *Palliative Care Formulary*, 5th Edition (PCF5)
- Major P, Lortholary A et al. (2001) Zoledronic Acid is Superior to Pamidronate in the treatment of Hypercalcaemia of Malignancy: a Pooled Analysis of Two Randomized, Controlled Clinical Trials. *Journal of Clinical Oncology*. **19**(2): 558-567.
- Rosen LS, Gordon D et al. (2003) Long-term Efficacy and Safety of Zoledronic Acid Compared with Pamidronate Disodium in the Treatment of Skeletal Complications in Patients with Advanced Multiple Myeloma or Breast Cancer. *Cancer*. **98**(8): 1735-1743.
- Stewart AF. (2005) Hypercalcaemia associated with cancer. *NEJM*. **352**(4): 373-379
- Society for Endocrinologists. 2013. *Acute Hypercalcaemia: Emergency Endocrine Guidance* [accessed October 8th 2015] https://www.endocrinology.org/policy/docs/13-02_EmergencyGuidance-AcuteHypercalcaemia.pdf

Management of Hypercalcaemia of Malignancy

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

Signs and Symptoms of Hypercalcaemia

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



Title of Guideline: Management of Hypercalcaemia of Malignancy

Date of Submission: November 2015

Date of Review: November 2017

Cockcroft Gault Calculation

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

* 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