

## Guideline for the management of HYPERCALCAEMIA in adults

### Definition(s)

HIGH serum adjusted calcium level

- **MILD** hypercalcaemia - adjusted serum calcium of **2.65 to 3.0 mmol/L**: often asymptomatic and does not usually require urgent correction.
- **MODERATE** hypercalcaemia - adjusted serum calcium of **3.0 to 3.5 mmol/L**: may be well tolerated if it risen slowly, but may be symptomatic and prompt treatment is usually indicated
- **SEVERE** hypercalcaemia - adjusted serum calcium of **over 3.5 mmol/L**: requires urgent correction due to the risk of dysrhythmia and coma

**Note that ALL patients with a adjusted serum calcium of 2.65mmol/L or over with known malignancy are managed as SEVERE**

### Potential Causes

**Ninety percent of hypercalcaemia is due to primary hyperparathyroidism or malignancy**

Other less common causes include:

- Familial hypocalciuric hypercalcaemia
- Non-malignant granulomatous disease
- Thyrotoxicosis
- Tertiary hyperparathyroidism
- Hypervitaminosis D
- Rhabdomyolysis
- Immobilisation
- Adrenal insufficiency
- Milk-alkali syndrome
- Hypervitaminosis A
- Pheochromocytoma
- Drugs
  - diuretics
  - lithium
  - theophylline
  - calcium and/or Vitamin D containing preparations eg. adcal, colecalciferol

If taking drugs that may be causative or contributory reduce or stop if suitable and re-check calcium THREE weeks after stopping drug.

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|------------------------|---|----------------------|-------------|
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### Signs and symptoms

Signs & symptoms may include:

- Polyuria and thirst
- Anorexia, nausea and constipation
- Mood disturbance, cognitive dysfunction, confusion and coma
- Renal impairment
- Shortened QT interval and dysrhythmias
- Peptic ulceration
- Hypertension, cardiomyopathy
- Muscle weakness

### Initial Actions

- Identify and manage underlying cause if possible.
- Stop any offending drugs
- Assess for cognitive impairment
- Determine fluid balance status
- Determine adjusted calcium level and use flow diagram below to determine management option
- Measure:
  - Urea
  - Creatinine
  - Phosphate

In addition, the following should be carried out to enable longer term management plan and further action. The result of these is NOT required before commencing treatment:

- Myeloma screen
- Parathyroid Hormone level

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## MANAGEMENT OF HYPERCALCAEMIA

**MILD HYPERCALCAEMIA**  
Serum Adjusted Calcium 2.65  
to 3.0mmol/L

**MODERATE HYPERCALCAEMIA**  
Serum adjusted Calcium  
3.1mmol/L and 3.5mmol/L

**SEVERE HYPERCALCAEMIA**  
Serum adjusted Calcium over 3.5mmol/L  
and **ALL patients with known malignancy**

Rehydrate using fluids (usually Sodium Chloride 0.9%) This will usually be FOUR to SIX Litres over 24 hours

After 24 hours assess fluid status and assess if further fluids are required. After 24 to 48hours measure corrected calcium. If further treatment is required consider Bisphosphonate. Maintain adequate hydration throughout.

**PLUS**

### ADMINISTER INTRAVENOUS BISPHOSPHONATE

Treat **ALL** patients with known malignancy as **SEVERE** irrespective of serum adjusted calcium level

#### Option1: Zoledronic Acid

#### **MILD and MODERATE HYPERCALCAEMIA)**

- Administer appropriate dose (below) in 100mL of glucose 5% or sodium chloride 0.9%

| Baseline CrCl      | Dose  |
|--------------------|-------|
| Over 60mL/min      | 4mg   |
| 50 to60 mL/min     | 3.5mg |
| 40to49 mL/min      | 3.3mg |
| 30 to 39 mL/min    | 3.0mg |
| Less than 30mL/min | avoid |

- Administer via intravenous (IV) infusion over at least 15 minutes.

#### Option 2: Disodium Pamidronate

#### **MILD HYPERCALCAEMIA**

30mg - Add to at least **250mL** of sodium chloride 0.9% or glucose 5%

| Baseline CrCl    | Infusion duration           |
|------------------|-----------------------------|
| Over 60mL/min    | 30 minutes                  |
| 11 to 60mL/min   | 90 minutes                  |
| 10mL/min or less | Consult renal drug handbook |

#### **MODERATE HYPERCALCAEMIA**

60mg - Add to at least **250mL** of sodium chloride 0.9% or glucose 5%

| Baseline CrCl    | Infusion duration           |
|------------------|-----------------------------|
| Over 60mL/min    | 60 minutes                  |
| 11 to 60mL/min   | 180 minutes                 |
| 10mL/min or less | Consult renal drug handbook |

### ADMINISTER INTRAVENOUS BISPHOSPHONATE

#### Option1: Zoledronic Acid

- Administer appropriate dose (below) in 100mL of glucose 5% or sodium chloride 0.9%

| Baseline CrCl      | Dose  |
|--------------------|-------|
| Over 60mL/min      | 4mg   |
| 50 to60 mL/min     | 3.5mg |
| 40to49 mL/min      | 3.3mg |
| 30 to 39 mL/min    | 3.0mg |
| Less than 30mL/min | avoid |

- Administer via intravenous (IV) infusion over at least 15 minutes.

#### Option 2: Disodium Pamidronate

- Dose - 90mg add to at least **500mL** of sodium chloride 0.9% or glucose 5%
- Administer the infusion at a rate based on renal function as stated below

| Baseline CrCl    | Infusion duration           |
|------------------|-----------------------------|
| Over 60mL/min    | Four hours                  |
| 11 to 60mL/min   | TWO hours                   |
| 10mL/min or less | Consult renal drug handbook |

- If patient has multiple myeloma or tumour induced hypercalcaemia, infuse disodium pamidronate over FOUR hours

Also continue further fluids if appropriate

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### Monitoring Requirements

- Whilst an inpatient, daily monitoring of:
  - sodium
  - potassium
  - magnesium
  - urea
- Whilst an inpatient, monitoring of Calcium after 48 hours (NADIR 2-4 days).

In addition, the following should be carried out to enable longer term management plan and further action. the result of these is NOT required before commencing treatment

- Myeloma screen
- Parathyroid Hormone level

**Conduct an ECG look for shortened QT interval or other conduction abnormalities.**

### Other Information

- The most common reason for severe hypercalcaemia is malignancy
- It is prescriber preference as to whether to use zoledronic acid or disodium pamidronate.
- Maximum treatment dose is 90mg of disodium pamidronate.
- A further dose of Zoledronic acid is NOT recommended within FOUR weeks. Seek specialist advice.
- If a raised Parathyroid Hormone Level - REFER for urgent parathyroidectomy
- Can prevent recurrence by:
  - Determining and treating the underlying cause
  - Maintenance treatment with bisphosphates (if untreatable malignancy)

### References

British National Formulary <https://bnf.nice.org.uk/>

Renal drug database <https://renaldrugdatabase.com/>

Summary of Product Characteristics <https://www.medicines.org.uk/emc/>

IV guide <https://medusa.wales.nhs.uk/> user name – cddward password- ivguide

Society for endocrinology endocrine emergency guidance - emergency management of acute hypercalcaemia in adult patients <https://ec.bioscientifica.com/view/journals/ec/5/5/G9.xml>

NICE CKS <https://cks.nice.org.uk/hypercalcaemia>

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