NHS
Kent and Medway

# Hypomagnesaemia in Adults – Primary Care Guide


Summary

- Hypomagnesaemia can be serious and potentially fatal when there is severe deficiency.
- Hypomagnesaemia has been reported in association with **all** proton pump inhibitors (PPIs) and other drugs such as diuretics.
- Two or more risk factors for hypomagnesaemia (see table below) should warrant magnesium (Mg) monitoring, particularly if patient is taking a PPI plus diuretic or if hypokalaemia and hypocalcaemia are evident.
  - Request for serum magnesium concentration (alongside other blood tests where possible).
- Request for serum magnesium concentration where there is suspicion of hypomagnesaemia and in patients who are also taking digoxin (hypomagnesaemia increases the risk of digoxin toxicity).


## Background

The April 2012 issue of the MHRA Drug Safety Update[1] (DSU) includes an article regarding hypomagnesaemia associated with the use of proton pump inhibitors (PPIs) (http://www.mhra.gov.uk/Safetyinformation/DrugSafetyUpdate/CON149774).

The advice suggests:

- Consider measurement of magnesium levels before starting PPI treatment and periodically during prolonged treatment, especially in those who will take a PPI concomitantly with digoxin or with drugs that may cause hypomagnesaemia (e.g. diuretics).
- Take into account any use of PPIs obtained over-the-counter.

## Risk factors or causes

| Medical conditions/circumstances | Drugs |
|---|---|
| Malnutrition or malabsorption<br>Chronic diarrhoea<br>Lactation or pregnancy<br>Anorexia nervosa<br>Chronic alcoholism<br>Refeeding syndrome<br>Acute pancreatitis<br>Diabetes/diabetic ketoacidosis<br>Renal defects (e.g. renal tubular reabsorption defects)<br>Genetic syndromes (e.g. Gitelman) | Proton pump inhibitors (PPIs)<br>Diuretics<br>Theophylline<br>Immunosuppressants (e.g. tacrolimus, ciclosporin)<br>Chemotherapy drugs (particularly cisplatin) |

Which patients are at higher risk of hypomagnesaemia?

Individuals with two or more risk factors, taking concomitant digoxin or have hypokalaemia and hypocalcaemia are likely to be at high risk. These patients should be prioritised for magnesium monitoring.

It has been suggested that higher dose PPI therapy may be linked to the development of hypomagnesaemia, as has longer duration of treatment and good adherence to therapy.


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## Signs and symptoms

Most patients with hypomagnesaemia are asymptomatic with symptoms more common when serum concentrations are <0.5mmol/L.[2] Symptoms, however, may occur in those with concentrations between 0.5 and 0.7mmol/L.

Neuromuscular effects: muscle weakness, ataxia, tremor, spasms of hands and feet.

Cardiovascular effects: arrhythmias, ECG abnormalities.

Other effects: seizures (especially children), coma, metabolic effects, confusion, delirium, fatigue, dizziness, nausea, vomiting.

Hypomagnesaemia is often associated with hypocalcaemia and hypokalaemia.

**Serum magnesium concentrations ≤0.4 mmol/L will be phoned by the laboratory to the requesting location or out of hours service, consider urgent admission in these cases (especially if acute onset or symptomatic).**

## Investigations and management

- For asymptomatic or mild hypomagnesaemia review the patient for the underlying cause. Most commonly this will be due to recent losses i.e. diarrhoea or medications.
- If appropriate, stop medications which may cause hypomagnesaemia. Seek specialist advice if necessary if drug cannot be stopped.
  ***If the patient was being treated with a PPI then review the need for this and if treatment needs to continue then switch to an H2 antagonist (e.g. famotidine, nizatidine, cimetidine).***
- PPIs are available over the counter. Check if the patient may be using these.
- For magnesium replacement options see below. Avoid using unlicensed products.
- For patients with recurring deficiencies please consider monitoring as appropriate. (Please also see below for advice on magnesium containing foods).

<table>
<tr><td colspan="3">Reference range 0.7-1.0mmol/L</td></tr>
<tr><th>Serum Mg (mmol/L)</th><th>Recommendation</th><th>Treatment</th></tr>
<tr><td>Mild deficiency:<br>0.51-0.69 mmol/L without symptoms</td><td>Consider oral replacement if there is a clinical concern (e.g. if ≥ 2 risk factors or acutely unwell)</td><td rowspan="3">(1st line) Magnaspartate® (Magnesium aspartate)[3]<br>1 sachet (10 mmol) OD or BD<br><br>OR<br><br>(2nd line) Neomag® (Magnesium glycerophosphate)[4]<br>1 (4 mmol) or 2 chewable tablet(s) TDS<br><br><u>Please prescribe by brand.</u></td></tr>
<tr><td>Mild deficiency:<br>0.51-0.69 mmol/L with symptoms</td><td rowspan="2">Requires oral replacement</td></tr>
<tr><td>Moderate deficiency:<br>0.41-0.5 mmol/L without symptoms<br>(if on digoxin see below)</td></tr>
<tr><td>Moderate deficiency:<br>0.41-0.5 mmol/L with symptoms (with or without symptoms for those on digoxin)</td><td>Usually requires IV replacement</td><td>Refer urgently for IV magnesium sulphate</td></tr>
<tr><td>Severe deficiency: ≤0.4 mmol/L</td><td>Requires IV replacement</td><td>Refer urgently for IV magnesium sulphate</td></tr>
</table>

*Refer to the Summary of Product Characteristics for further details on prescribing.*

## Replacement advice

Magnesium replacement should be used with caution in patients with myasthenia gravis, patients with hepatic impairment at risk of developing renal impairment, patients with renal impairment and respiratory insufficiency.

Avoid or significantly reduce doses of magnesium salts in patients with severe renal impairment (eGFR <30 mL/minute/1.73$^2$) - monitor for signs of hypermagnesaemia and re-check serum magnesium concentrations. This is an off-licence use.

Oral magnesium salts commonly cause gastrointestinal irritation. Treatment is often poorly tolerated being limited by diarrhoea so advise to take with meals and separation of dosing.

For patients with normal renal function it is advisable to continue magnesium supplementation for one to two days after serum magnesium concentration has normalised. (Intracellular stores take longer to replete).

Where medication induced hypomagnesaemia is considered to be serious this should be reported to the MHRA via the Yellow Card system.

## Advice for patients

Patients should be aware of and advised to report symptoms of hypomagnesaemia to a healthcare professional.

Many common foods contain magnesium including green vegetables, wholemeal bread, wholemeal pasta, nuts, pulses such as kidney beans and lentils, soya beans, peas, baked beans, seafood. "Hard" water also contains magnesium salts.

## Other uses of magnesium preparations

*It is not advisable to prescribe magnesium routinely unless there is a clinical need such as medically diagnosed deficiency or lifelong/chronic condition that may result in malabsorption. Continuing need should be reviewed on a regular basis.*[5]

*Patients should be encouraged to purchase magnesium supplements over the counter unless the above exceptions apply.*

References


1. MHRA Drug Safety Update. http://www.mhra.gov.uk/Safetyinformation/DrugSafetyUpdate/CON149774
2. Ayuk J and Gittoes NJL. How should hypomagnesaemia be investigated and treated? Clin. Endocrinol (Oxf). 2011 Dec; 75(6):743-6
3. Magnaspartate® Summary of Product Characteristics. Magnaspartate 243mg Powder for Oral Solution - Summary of Product Characteristics (SmPC) - (emc) (medicines.org.uk)
4. Neomag® Summary of Product Characteristics Neomag - Summary of Product Characteristics (SmPC) - (emc) (medicines.org.uk)
5. NHS England Conditions for which over the counter items should not routinely be prescribed in primary care: Guidance for CCGs. March 2018. otc-guidance-for-ccgs.pdf (england.nhs.uk)



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