SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Neomag 4mmol chewable tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each chewable tablet contains magnesium glycerophosphate equivalent to 4mmol (97mg) of magnesium.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Chewable tablet

A white, round, flat tablet, cross-scored on one face. The score line is only to facilitate breaking for ease of swallowing and not to divide into equal doses.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Neomag 4mmol Chewable Tablets are indicated as oral magnesium supplements for the treatment of patients with chronic magnesium loss or hypomagnesaemia as diagnosed by a doctor.

Neomag 4mmol Chewable Tablets are also indicated for adult patients with hypomagnesaemia due to the concomitant administration of loop and thiazide diuretics or other drugs which cause hypomagnesaemia.

4.2 Posology and method of administration

Posology

Patients with severe, symptomatic hypomagnesaemia should receive intravenous magnesium repletion for acute recovery of magnesium levels prior to receiving Neomag.

It is recommended that serum magnesium levels should be monitored at regular intervals (e.g. every 3-6 months), particularly in children and in patients with renal impairment.

Adults (> 18 years): The dosage regimen should be adjusted according to the serum total magnesium level of the individual patient. Starting doses for adult patients are recommended as 4-8 mmol (1-2 tablets) administered 3 times a day. This equates to a total dose of 12 to 24 mmol per day taken in divided doses.

Elderly: No dose adjustment is necessary.

Children: Neomag tablets should only be used if the benefits of treatment outweigh any potential risks and under the supervision of physicians experienced in the management of children with hypomagnesaemia.

Children: below 4 years: Not recommended as there is insufficient information regarding the use of Neomag tablets in this age group.

Children: 4 to 12 years: The dosage regimen should be adjusted according to the serum total magnesium level of the individual patient. A starting dose for children 4 to 12 years is recommended as 4 mmol (1 tablet) administered 2 times a day. This equates to a total dose of 8 mmol per day taken in divided doses.

Children: 12 to 18 years: The dosage regimen should be adjusted according to the serum total magnesium level of the individual patient. A starting dose for children 12 to 18 years is recommended as 4 mmol (1 tablet) administered 3 times a day. This equates to a total dose of 12 mmol per day taken in divided doses.

Patients with Renal Impairment: Neomag is contraindicated in patients with severe renal impairment (see Section 4.3). There is no dose adjustment necessary in patients with mild to moderate renal impairment.

Method of administration

The tablet may be broken into quarters and chewed or swallowed with water.

Co-Administration of Potassium and Calcium Supplements: Administration of potassium and calcium together with magnesium may be necessary since associated loss of these cations is common in severe magnesium deficiency.

4.3 Contraindications

Neomag is contraindicated in patients with severe renal impairment (glomerular filtration rate <30ml/min).

Neomag should not be administered to patients with phenylketonuria as Neomag tablets contain Aspartame.

Neomag should not be administered to patients with hyperphosphataemia as Neomag tablets contain phosphate.

Do not administer Neomag tablets if there is evidence of hypersensitivity to any of the constituents.

4.4 Special warnings and precautions for use

The principle sites of absorption of magnesium in the gastrointestinal tract are the jejunum and ileum, therefore, in patients who have undergone extensive bowel resection the absorption of magnesium may be reduced.

In the case of confirmed magnesium deficiency, concomitant hypocalcaemia and hypokalaemia should be suspected and corrected if confirmed, since magnesium deficiency is frequently secondary to those conditions.

4.5 Interaction with other medicinal products and other forms of interaction

Cardiovascular drugs: Digoxin and loop diuretics are magnesiuretic drugs and may affect magnesium balance. Magnesium deficiency may enhance digoxin toxicity.

As magnesium and other medicinal products may mutually influence each other's absorption, a time interval of 2 to 3 hours should generally be respected if possible.

This specifically applies to:

- **Cellulose sodium phosphate; edetate disodium**: concurrent use with magnesium supplements may result in binding of magnesium; patients should be advised not to take magnesium supplements within 1 hour of cellulose sodium phosphate or edentate disodium.
- **Fluorides and tetracycline**: if they must be used, the doses must be separated by 2 to 3 hours or more to prevent their admixture in the gut.
- **Aminoquinolines, quinidine and quinidine derivatives, nitrofurantoin, penicillamine, iron, bisphosphonates (such as alendronate and risedronate), eltrombopag, nitroxoline**: to avoid impairment of absorption, magnesium preparations should be taken 3 to 4 hours before or after the administration of those drugs.

Because of increased magnesium losses, a dose adjustment of magnesium may be necessary when taking the following substances:

- Aminoglycoside antibiotics, cisplatin and ciclosporin A
- Diuretics (such as thiazide and furosemide),
- EGF-receptor antagonists (such as cetuximab and erlotinib),
- proton pump inhibitors (such as omeprazole and pantoprazole) and
- viral DNA polymerases-inhibiting foscarnet, pentamidine, rapamycin and amphotericin B

In addition, other electrolyte disturbances, such as hypokalaemia and hypocalcaemia, should be looked for in these patients with hypomagnesaemia.

For further information on mechanisms of drug interactions see section 5.2.

4.6 Fertility, pregnancy and lactation

Pregnancy

The effectiveness and safety of Neomag has not been established in pregnant women. Neomag tablets should only be used in pregnancy if the benefits of the treatment outweigh any potential risks. However, long-term data available from treatment of pre-eclampsia do not indicate malformative or feto/neonatal toxicity of magnesium.

Administration of aminoglycoside antibiotics should be avoided during this period, as there are indications of interactions (see Section 4.5).

Lactation

Neomag can be used during breast-feeding. Magnesium glycerophosphate /its metabolites are excreted in human milk, but at therapeutic doses of Neomag no effects on the breastfed newborns/infants are anticipated.

Fertility

Based on long-term experience, no effects of magnesium on male and female fertility are anticipated.

4.7 Effects on ability to drive and use machines

Neomag has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

As with other magnesium salt preparations, Neomag may cause diarrhoea, which is usually dose dependant. If diarrhoea occurs, the daily dose should be reduced and gradually increased later if needed.

Hypermagnesaemia is possible with higher doses and with impaired renal function.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme at www.mhra.gov.uk/yellowcard.

4.9 Overdose

Symptoms: Hypermagnesaemia characterised by flushing, thirst, hypotension, drowsiness, nausea, vomiting, confusion, loss of tendon reflexes due to

neuromuscular blockade, muscle weakness, respiratory depression, cardiac arrhythmias, coma and cardiac arrest.

Treatment of Iatrogenic Hypermagnesaemia and Overdose: When hypermagnesaemia is found, magnesium therapy should be withdrawn and this is all that is needed in most patients with mild to moderate hypermagnesaemia. In patients with symptomatic hypermagnesaemia, serum magnesium should be lowered and the effects of hypermagnesaemia antagonised. Calcium antagonises the toxic effects of magnesium and therefore patients with severe magnesium intoxication should be given intravenous calcium gluconate as a bolus followed by an infusion. Administration of glucose and insulin may also help to promote magnesium entry into cells. If renal function is normal adequate fluids should be given to assist removal of magnesium from the body. If the patient is in renal failure, peritoneal or haemodialysis against a low magnesium dialysis fluid will rapidly and effectively lower the serum magnesium concentration.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Mineral supplements, ATC code: A12CC.

Magnesium is the second most abundant cation in intracellular fluid and is an essential body electrolyte. Magnesium is a factor in a number of enzyme systems, and is involved in neurochemical transmission and muscular excitability.

Supplements containing magnesium have been shown to be of use in restoring a magnesium deficit in humans. Given the central role that magnesium plays in human metabolism, magnesium replacement in the presence of a deficiency is an appropriate therapeutic action to take. This is particularly important given the significant clinical problems that can arise as a result of hypomagnesaemia in relation to the cardiovascular and neurological systems.

5.2 Pharmacokinetic properties

The relative bioavailability of Neomag has been determined in a Phase I clinical study.

The specific regimen for magnesium supplementation is dependent on clinical presentation. Symptoms of magnesium deficiency i.e. <0.7mmol/l should be treated empirically and adjusted according to response and tolerance. Magnesium absorption may take a few days to return to reference levels and intravenous magnesium may need to be considered for severe cases of hypomagnesaemia.

Normal serum magnesium ranges between 0.75–0.95 mmol/l at any age and approximately 20% of this is bound to albumin in the intravenous compartment. Even though 80% of serum magnesium is filtered at the glomerulus, only 3% of it is finally excreted in the urine. Intravenous or oral magnesium repletion is the main treatment for hypomagnesaemia, and potassium-sparing diuretics may also induce renal magnesium saving. Because the kidney has a very large capacity for

magnesium excretion, hypermagnesaemia usually occurs in the setting of renal insufficiency and excessive magnesium intake.

Absorption and Distribution: Normal magnesium body content is around 25g and 60–65% of it is located in the bone. The recommended magnesium dietary content for adults is approximately 250mg/day (62.5mmol/day) in men and 200mg/day (50mmol/day) in women. Of the total amount ingested, approximately one third is eliminated in the urine and the remainder in the faeces. A small amount of magnesium (15 to 30 mg/day) is secreted into the gastrointestinal tract. Magnesium homeostasis involves the kidney, small bowel and bones. In the gastrointestinal tract, magnesium absorption occurs primarily in the jejunum and ileum. Under basal conditions the small intestine absorbs 30–50% of magnesium intake, although this percentage diminishes with increasing amount of magnesium intake and chronic renal disease.

Renal Excretion: The major excretory pathway for absorbed magnesium is through the kidney. The renal excretion of magnesium is about 120 to 140mg/24hours for an adult on a normal diet. Thus, the amount of magnesium absorbed from the small intestine is similar to the amount excreted by the kidney for a person in normal magnesium balance. The kidney is the major organ that controls the magnesium concentration in the serum. Renal excretion is determined largely by the rate of filtration and its tubular re-absorption, while tubular secretion does not seem to play a significant role in its renal handling. Between 10 and 15% of filtered magnesium is re-absorbed in the proximal convoluted tubules, while 60–70% is passively re-absorbed in the thick ascending loop of Henle. In the distal convoluted tubules, magnesium re-absorption is still significant and represents the fine regulation of its excretion.

Magnesium homeostasis influenced by medical conditions

Excessive excretion of magnesium into the urine is a cause of magnesium depletion. Osmotic diuresis due to glucosuria can result in magnesium depletion, and diabetes mellitus is probably the most common clinical disorder associated with magnesium depletion. Therefore, diabetics have an increased requirement for magnesium. Magnesium deficiency has been shown to result in cardiovascular disorders such as cardiac dysrhythmias, which may be manifested by a rapid heart rate (tachycardia), skipped heart beats (premature beats), or a totally irregular cardiac rhythm (fibrillation). A low magnesium status leads to arterial vasoconstriction and thrombocyte aggregation. Migraine patients often show low magnesium levels, therefore, magnesium deficiency seems to play a role in the pathogenesis of migraine. Magnesium supplementation was effective in migraine prophylaxis.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential, toxicity to reproduction and development.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Maize starch, microcrystalline cellulose, talc, aspartame, magnesium stearate, colloidal anhydrous silica, povidone.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Do not store above 25°C. Do not freeze. Store in the original packaging.

6.5 Nature and contents of container

Polypropylene plastic bottles with LDP/HDP blend caps containing 50 chewable tablets.

6.6 Special precautions for disposal

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Neoceuticals Limited

The Innovation Centre

Innovation Way

Heslington

York

YO10 5DG

8 MARKETING AUTHORISATION NUMBER(S)

PL 36116/0003

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

10/01/2017

10 DATE OF REVISION OF THE TEXT

10/01/2017