SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)

1. NAME OF THE MEDICINAL PRODUCT

Magnesium Sulfate Injection BP – MAGSPEC INJECTION

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Qualitative declaration

Magnesium Sulfate Heptahydrate 50% w/v (approximately 2 mmol Mg2+ /mL)

Quantitative declaration

Excipients with known effect

For full list of Excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for Injection

Distribution Category: POM

A clear colourless solution.

4. CLINICAL PARTICULARS

1. Therapeutic Indications

It is indicated in the treatment of magnesium deficiency in hypomagnesaemia where the oral route of administration may be inappropriate. It is also indicated to prevent further seizures associated with fulminant pre-eclampsia, Eclampsia.

2. Posology and Method of Administration

Route of administration: It may be administered by intramuscular (IM) or intravenous routes (IV). Intramuscular (IM) therapy should be used only when peripheral venous access is impossible.

Dose equivalence and conversion: Magnesium sulfate heptahydrate 1 g equivalent to Mg2+ approx. 4 mmol.

Intramuscular Regimen: 4 g (approx. 16 mmol Mg2+) IV (usually in 20% solution) Slowly over 5 minutes (minimum, preferably 10-15 min) is followed immediately by 5 g (usually in 50% solution) as a deep IM injection into the upper outer quadrant of each buttock.

Intravenous Regimen: 4 g (approx. 16mmol Mg2+) IV over up to 20 minutes followed by an intravenous rate of 1g every hour continued for 24h after the last fit.

Recurrent Convulsions: In both the IM and IV regimens, if convulsions recur, a further 2-4 g (approx. 8 - 16mmol Mg2+) (depending on the woman's weight, 2 g (approx. 8mmol Mg2+) if less than 70Kg) is given IV over 5 min.
Dosage should be individualized according to patient's needs and responses. Plasma levels should also be monitored throughout therapy.

Treatment of magnesium deficiency in hypomagnesaemia:
For IV: A concentration of 20% or less should be used; the rate of injection not exceeding 1.5 ml/minute of a 10% solution or its equivalent. Up to 40 g (equivalent

to 160mmol Mg^{2+}) by slow intravenous infusion (in glucose 5%) over up to 5 days, may be required to replace the deficit (allowing for urinary losses).
Mild magnesium deficiency: 1g intramuscularly every 6 hours for 4 doses.
Severe magnesium deficiency: Up to 250 mg/kg (IM) given within a period of 4 hours or 5g/litre of infusion solution (IV) over 3 hours.

Paediatric population: It is recommended that the solution be diluted to 20% w/v prior to intramuscular injection
Elderly: No special recommendation except in renal impairment.

Renal impairment: Dosage should be reduced. Plasma magnesium concentrations should be monitored throughout therapy

Dilution Pattern: Dilution should be done according to the dosage requirement. For intramuscular use, a 25% or 50% solution is used. For intravenous use, this solution must be diluted before use. Concentrations of up to 20% are usually employed. Preparation of 20% solution of 4 mg magnesium sulphate from 50% solution: Take 8ml of 50% magnesium sulphate injection solution and add 12ml of 5% Dextrose or 0.9% saline solution to make-up the total volume upto 20 ml in a sterile injection. Discard any unused solution immediately after first use. From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage time and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2-8°C, unless dilution has taken place in controlled and validated aseptic conditions.

3. Contraindications

It is contraindicated in patients with hypersensitivity to magnesium and its salts or to any of the excipients. It is also contraindicated in patients with severely impaired renal function.

4. Special Warnings and Special Precautions for Use

It must be used with caution in patients suspected of or known to have renal impairment.
It should not be used in hepatic coma if there is a risk of renal failure. Parenteral magnesium salts should be used with caution in patients with myasthenia gravis. Serum calcium levels should be routinely monitored in patients receiving magnesium sulfate.

Pregnancy: It crosses the placenta. When used in pregnant women, foetal heart rate should be monitored and use within 2 hours of delivery should be avoided. It can cause skeletal adverse effects when administered continuously for more than 5 to 7 days to pregnant women. Based on studies reports fetal abnormalities with maternal administration of magnesium sulphate beyond 5 to 7 days. The clinical significance of the observed effects is unknown. If prolonged or repeated exposure to magnesium sulfate occurs during pregnancy monitoring of neonates for abnormal calcium or magnesium levels and skeletal adverse effects should be considered. These abnormalities include skeletal demineralization and osteopenia. It should be used during pregnancy only if clearly needed.

Lactation: It is not advisable to administer magnesium sulfate during breastfeeding unless considered essential, and it must be administered under medical supervision.
Hepatic Impairment: Avoid in hepatic coma if risk of renal failure.
Renal Impairment: Increased risk of toxicity. Dose adjustments: Avoid or reduce dose.

5. Interaction with other medicinal products and other forms of interaction

Administer with caution to patients receiving digitalis glycosides. Magnesium sulfate should not be administered concomitantly with high doses of barbiturates, opiods or hypnotics due to the risk of respiratory depression. The action of non-depolarising muscle relaxants such as tubocurarine is potentiated and prolonged by parenteral magnesium salts. Concomitant use of calcium channel blockers such as nifedipine or nimodipine may rarely lead to a calcium ion imbalance and could result in abnormal muscle function. The neuromuscular blocking effects of parenteral magnesium and aminoglycoside antibacterials may be additive.

4.6 Pregnancy and Lactation

Pregnancy: It crosses the placenta. When used in pregnant women, foetal heart rate should be monitored and use within 2 hours of delivery should be avoided. It can cause skeletal adverse effects when administered continuously for more than 5 to 7 days to pregnant women. Based on studies reports fetal abnormalities with maternal administration of magnesium sulphate beyond 5 to 7 days. The clinical significance of the observed effects is unknown. If prolonged or repeated exposure to magnesium sulfate occurs during pregnancy monitoring of neonates for abnormal calcium or magnesium levels and skeletal adverse effects should be considered. These abnormalities include skeletal demineralization and osteopenia. It should be used during pregnancy only if clearly needed.

Lactation: It is not advisable to administer magnesium sulfate during breastfeeding unless considered essential, and it must be administered under medical supervision.

4.7 Effects on ability to Drive and use Machines

No studies on the effects on the ability to drive and use machines have been performed.

8. Undesirable Effects

The adverse effects of parenterally administered magnesium usually as follow: Metabolism and nutrition disorders. Electrolyte/fluid abnormalities (hypophosphataemia, hypertonic dehydration). Hypersensitivity reactions. Hypocalcaemia. Pain or burning at the injection site following IV/IM administration. Hypermagnesaemia characterised by flushing, sweating, thirst, hypotension, drowsiness, dizziness, headache, risk ofitching and tingling, nausea, vomiting, confusion, slurred speech, double vision, loss of tendon reflexes due to neuromuscular blockade, muscle weakness, respiratory depression, electrolyte/ fluid abnormalities (hypophosphataemia, hyperosmolar dehydration), ECG changes (prolonged PR, QRS and QT intervals), bradycardia, tachycardia cardiac arrhythmias, coma and cardiac arrest. There have been isolated reports of maternal and fetal hypocalcaemia with high doses of magnesium sulfate.

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 to **TMDA**

9. Overdose

Symptoms: Hypermagnesaemia characterized by flushing, hypotension, drowsiness, nausea, vomiting, confusion, loss of tendon reflexes due to neuromuscular blockade, muscle weakness, respiratory depression, electrolyte/ fluid abnormalities, ECG changes, bradycardia, cardiac arrhythmias and cardiac arrest. Patients with renal failure and metabolic derangements develop toxicity at lower doses.

Treatment**:** Appropriate action should be taken to reduce the blood level of magnesium to avoid hypermagnesaemia. Neuromuscular blockade associated with hypermagnesaemia may be reversed with calcium salts, such as Calcium Gluconate, which should be administered intravenously in a dose equivalent to 2.5 to 5 mmol of calcium.

5. PHARMACOLOGICAL PROPERTIES

1. Pharmacodynamics Properties

Pharmacotherapeutic Group: Mineral Supplements

ATC code: A12CC02.

Magnesium is the second most abundant cation in intracellular fluid and is an essential body electrolyte. Increases osmotic gradient in small intestine, which draws water into intestines and causes distention. These effects stimulate peristalsis and bowel evacuation. In antacid action, reacts with hydrochloric acid in stomach to form water and increase gastric pH. It is a factor in a number of enzyme systems, and is involved in neurochemical transmission and muscular excitability. Parenterally administered magnesium sulfate exerts a depressant effect on the central nervous system and acts peripherally to produce vasodilation.

2. Pharmacokinetic Properties

Absorption: Intravenously administered magnesium is immediately absorbed. Following (IV) administration, the onset of action is immediate and last for approx. 30 minutes. (IM) administration, the onset of action occurs within 1 hour and the duration of action is 3 to 4 hours. Upon (IM) administration, the plasma concentration of magnesium sulfate shows a slow increase that reaches a plateau within 1 to 2 hours and is followed by a slow decline back to baseline within the next 6 to 8 hours. At the end of4 hours, after another intramuscular injection of magnesium sulfate, the plasma concentration remains constant.

Distribution: Plasma protein binding of injected magnesium is comparable to endogenous magnesium. About 40% to 50% of plasma magnesium is protein bound and not ultra-filterable approximately 1-2% of total body magnesium is located in the extracellular fluid space. The unbound magnesium ions diffuse into the extravascular-extracellular space, bones, cross the placenta and are rapidly taken up by foetal tissues and thus magnesium in amniotic fluid, the foetus and in

neonates of mothers treated with magnesium sulfate show increased concentrations as compared to untreated mothers. Magnesium is 30% bound to albumin. The mean baseline cerebrospinal fluid (CSF) magnesium level in pre-eclamptic women was 1.1 ±0.05mmol/L. Intrapartum magnesium sulfate treatment increased breast milk/colostrum magnesium levels significantly only for 24 hours. After 24 hours magnesium levels in breast milk comes back to normal. Breast milk/colostrum calcium levels were not affected by magnesium sulfate therapy.

Metabolism and Excretion: It is not metabolized and is excreted solely by the kidney. Urinary excretion is very rapid with a 20-fold increase during infusion. About 38 to 53% of the total injected magnesium is excreted 4 hours after the end of the infusion and >90% are eliminated within 24 hours after the infusion. In patients with normal renal function, the increase in magnesium clearance is linear to the serum magnesium concentrations and the half-life of magnesium is 4 hours. Half-life increases with decrease in glomerular filtration rate. Urinary calcium concentration increases 4.5-fold during infusion of magnesium sulfate and there is a 3- fold increase in urinary calcium excretion rate which is likely due to competition for common reabsorption sites.

3. Preclinical Safety Data

Effects in non-clinical studies were observed only at exposures considered sufficiently in excess of the human exposure indicating little relevance to clinical use.

6. PHARMACEUTICAL PARTICULARS

1. List of Excipients

Activated Charcoal BP
Water for injection BP

2. Incompatibilities

Not applicable.

3. Shelf Life

24 months

4. Special Precautions for Storage

Do not store above 30°C. Protect from light.

5. Nature and Contents of Container

A clear colourless solution filled in 10 ml glass ampoule. Such 5 ampoules are tray packed in printed carton with packing insert.

6. Special precaution for disposal and other handling

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORIZATION HOLDER AND MANUFACTURING SITE ADDRESSES

1. Name and Address of Marketing Authorization Holder

Lincoln Pharmaceuticals Limited
Trimul Estate, Khatraj, Taluka: Kalol,
District: Gandhinagar Gujarat, India.
Telephone no.: +91-79-41078096
Fax: +91-79-41078062
Email: hiren@lincolnpharma.com
Website: www.lincolnpharma.com

2. Name and Address of manufacturing site(s)

Lincoln Pharmaceuticals Limited
Trimul Estate, Khatraj, Taluka: Kalol,
District: Gandhinagar Gujarat, India.
Telephone no.: +91-79-41078096
Fax: +91-79-41078062
Email: hiren@lincolnpharma.com
Website: www.lincolnpharma.com

8. MARKETING AUTHORIZATION NUMBER

TAN 22 HM 0505

9. DATE OF FIRST <REGISTRATION> / RENEWAL OF THE <REGISTRATION>

05th December, 2022

10. **DATE OF REVISION OF THE TEXT**