# Magnesium sulfate for fetal neuroprotection UHL Obstetric guideline

University Hospitals of Leicester NHS Trust

**Trust ref: C3/2015**

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"Currently UHL utilises the terms ‘woman’ and ‘women’ within their obstetric and maternity guidelines but these recommendations will also apply to people who do not identify as women but are pregnant or have given birth."

## 1. Introduction and Who Guideline applies to

This guideline aims to assist clinicians caring for women presenting with established preterm labour, or planned preterm delivery at < 32 weeks gestation. It aims to inform clinicians when making a decision to administer Magnesium sulfate how and when to administer it.

### Background:

Cerebral palsy (CP) is a group of disorders characterised by non-progressive motor and/or postural dysfunction and cognitive impairment. The prevalence of CP is about 1 in every 400 children (2 to 2.5 per 1000 live births). However risk of CP is significantly higher in children born preterm: 15% of those born < 28 weeks, and 6% of those born at 28-31 weeks will develop cerebral palsy (RCOG 2011).

Several large trials have been undertaken to examine the effect of antenatally administered magnesium sulfate ($MgSO_4$) on the risk of CP in the surviving preterm baby (Crowther 2003, Rouse 2008, Marret 2007). The available evidence suggests that $MgSO_4$ given before anticipated early preterm birth reduces the risk of cerebral palsy by 32% (Doyle 2009). It is estimated that 46 women giving birth at < 30 weeks

gestation or 56 women giving birth at < 32 weeks gestation will need to be treated with $MgSO_4$ to prevent one case of cerebral palsy (RCOG 2011).

**Related guidelines:**

**Severe Pre Eclampsia and Eclampsia - UHL Obstetric Guideline**
**Preterm Labour Guidance in the Absence of PPROM UHL Obstetric Guideline**
**Pre Labour Rupture of the Membranes UHL Obstetric Guideline**

**NB. The Neonatal team should be aware of the antenatal administration of magnesium sulfate as it has the potential to alter the neonates' neurological evaluation.**

## 2. Indications for magnesium sulfate administration

- Magnesium sulfate administration should be considered for all women 24 – 31+6 weeks gestation in whom delivery is anticipated within 24 hours. This includes women in established preterm labour and for women for whom delivery is planned for fetal or maternal indications
- The decision to administer magnesium sulfate between 24 and 31+6 weeks gestation should be made by an ST6/ST7 Specialist Registrar or Consultant Obstetrician
- The Neonatal team should be aware of the antenatal administration of magnesium sulfate as it has the potential to alter the neonates' neurological evaluation
- Delivery **should not be delayed** in order to administer magnesium sulfate for fetal neuroprotection if there are maternal and / or fetal indications for emergency delivery (e.g. fetal compromise, antepartum haemorrhage or cord prolapse)
- For women between 23+0 and 23+6 weeks of pregnancy who are in established preterm labour or having a planned preterm birth within 24 hours, a discussion should be held with the woman, the obstetric consultant and neonatal team, regarding the use of intravenous magnesium sulfate for neuroprotection of the baby, in the context of her individual circumstances. NICE NG25 (2015 updated June 2022)
- Consideration for MgSO4 can be given to those at higher risk of cerebral palsy between 32-33+6. Previous cerebral palsy, IUGR, and multiple pregnancy, known anomaly.
- "Established preterm labour" should be defined as a high likelihood of birth within 24 hours with cervical dilatation of ≥ 4 cm, with or without preterm pre labour rupture of membranes (PPROM)
- Magnesium sulfate administration should be considered regardless of the reason for the preterm birth, whether singleton or multiple pregnancy or

the expected mode of delivery (vaginal birth or caesarean section)

## 3. Exclusion criteria:

Prior to a decision to administer magnesium sulfate a full assessment of the woman should be carried out. This should include confirmation that the woman does not meet the exclusion criteria.

Exclusion criteria;

- Magnesium sulfate already administered for pre eclampsia / eclampsia
- Magnesium sulfate contraindicated (Myasthenia Gravis)
- Hypersensitivity to the drug, hepatic coma
- Caution in maternal renal impairment
- Fetus unlikely to benefit (severe fetal malformations or chromosomal abnormalities)

## 4. Administration of magnesium sulfate

- Administration of magnesium sulfate should take place on the Delivery Suite with appropriate maternal and fetal monitoring

- Antenatal magnesium sulfate should be administered as an intravenous infusion on the Delivery Suite because of the potential for maternal respiratory depression, hypotension and fetal compromise

- Magnesium sulfate should be administered as per the flow chart (see Appendix 1)

- For planned preterm birth for fetal or maternal indications, magnesium sulfate should be commenced at least 4 hours before birth

- The magnesium sulfate infusion should be reviewed after 12 hours and may be stopped if delivery is no longer anticipated.

- Maternal Monitoring should include:

    - Maternal pulse, blood pressure, respiratory rate and patellar reflexes prior to the loading dose
    - Maternal pulse, blood pressure, respiratory rate and patellar reflexes at the end of the loading dose
    - Maternal pulse, blood pressure, respiratory rate and patellar reflexes hourly during the infusion
    - Maternal ECG during and for 1 hour after the loading dose

- Routine catheterisation is not required unless there is another indication, or unless concerns about inadequate urine output

- Routine monitoring of serum magnesium levels is not indicated
- Maternal blood should be taken for baseline renal function testing at commencement of infusion (commencement does not need to be delayed to await results). If there is evidence of renal impairment then consider halving the dose or discontinuing the infusion.
- Continuous electronic fetal monitoring should be undertaken if intervention would be considered for fetal reasons (as per the Preterm Labour Guideline)
- Antenatal corticosteroids should be administered for fetal lung maturation if not already given
- If magnesium sulfate is being administered for Pre Eclampsia then management should be as per the Severe Pre Eclampsia Guideline
- The Neonatal team should be aware of the antenatal administration of magnesium sulfate as it has the potential to alter the neonates' neurological evaluation

## 5. Tocolysis

- If magnesium sulfate has been commenced for fetal neuroprotection, then tocolysis should be discontinued
- If active labour has been diagnosed then in normal circumstances the tocolysis would be discontinued
- In exceptional circumstances administration of tocolytics and magnesium sulfate simultaneously may be considered (e.g. advanced dilatation at extreme preterm gestation with irregular contractions). The decision to do so must be made by the consultant. There is no evidence on the safety or otherwise of simultaneous administration of atosiban and magnesium sulfate.
- Nifedipine should also be used with caution in combination with magnesium sulphate to avoid precipitous fall of maternal blood pressure or adverse neuromuscular effects. Appropriate monitoring is advisable. Should they be administered simultaneously the magnesium sulphate bolus dose can be slowed down.

## 6. Toxicity

- Magnesium sulfate infusion for fetal neuroprotection should be discontinued if there are any signs of toxicity

- The infusion should be stopped if the respiratory rate decreases more than 4 breaths per minute below the baseline, or is less than 12 breaths per minute

- The infusion should be stopped if the diastolic blood pressure decreases by more than 15mm Hg below the baseline level

- If there are any signs of magnesium toxicity (see Appendix 2), the magnesium sulfate infusion should be stopped and managed according to Appendix 2. It should only be restarted if it is required due to severe pre-eclampsia/eclampsia.

## 7. Repeat doses

- There is no evidence regarding repeated doses of magnesium sulfate. However there will be occasions where delivery does not occur after the initial dose.

- Magnesium sulfate may be repeated if >24 hours after discontinuation of previous MgSO4 and delivery now anticipated within 24 hours.

## 8. Education and Training

None

## 9. Audit standards

100% of eligible babies born at <32 weeks gestation should receive antenatal $MgSO_4$.

100% of women receiving $MgSO_4$ for fetal neuroprotection should also have received at least one dose of antenatal corticosteroid.

## 10. Supporting References

Doyle LW, Crowther CA, Middleton P, Marret S, Rouse D. Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus. Cochrane Database Syst Rev 2009;(1): CD004661.

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RCOG 2019 Green Top Guideline 73: care-of-women-presenting-with-suspected-preterm-prelabour-rupture-of-membranes-from-24plus0-weeks-of-gestation https://www.rcog.org.uk/guidance/browse-all-guidance/green-top-guidelines/care-of-women-presenting-with-suspected-preterm-prelabour-rupture-of-membranes-from-24plus0-weeks-of-gestation-green-top-guideline-no-73/

NICE 2015 (updated June 2022) NG25 Preterm labour and birth https://www.nice.org.uk/guidance/ng25/chapter/Recommendations#magnesium-sulfate-for-neuroprotection

## 11. Key Words

Cerebral palsy, Neonatal, Preterm

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**The Trust recognises the diversity of the local community it serves. Our aim therefore is to provide a safe environment free from discrimination and treat all individuals fairly with dignity and appropriately according to their needs.**
**As part of its development, this policy and its impact on equality have been reviewed and no detriment was identified.**

| CONTACT AND REVIEW DETAILS | | | |
|---|---|---|---|
| **Guideline Lead (Name and Title)**<br>P McParland – Consultant Obstetrician | | | **Executive Lead**<br>Chief Nurse |
| **Details of Changes made during review:** | | | |
| **Date** | **Issue Number** | **Reviewed By** | **Description Of Changes (If Any)** |
| **May 2019** | **V2** | **P McParland** | Use of calcium gluconate for cardio pulmonary arrest added<br>Mag Sulf may be repeated if >24 hours after discontinuation of previous mag sulf and delivery now anticipated added<br>Mag sulf infusion should be reviewed after 12 hours and may be stopped if delivery no longer anticipated |
| **November 2022** | **V3** | **S Dunkerton** | Updated advice regarding individualised discussion at 23-23+6 gestation in line with NICE NG25<br>Added - Consideration for MgSO4 can be given to those at higher risk of cerebral palsy between 32-33+6. Previous cerebral palsy, IUGR, and multiple pregnancy, known anomaly.<br>Maternal monitoring – added Maternal ECG during and for 1 hour after the loading dose<br>Added statement - Nifedipine should also be used with caution in combination with magnesium sulphate to avoid precipitous fall of maternal blood pressure or adverse neuromuscular effects. Appropriate monitoring is advisable. Should they be administered simultaneously the magnesium sulphate bolus dose can be slowed down.<br>Update magnesium infusion preparation and administration |

## Appendix 1: Intravenous administration of magnesium sulfate

| | |
|---|---|
| **Loading dose** | 4g Magnesium sulfate given over 15 - 30 minutes to be administered by medical staff.<br>NB: In extreme emergencies the loading dose may be administered by an experienced midwife who feels confident and competent to do so.<br><br>Prepare infusion solution by drawing up 20ml of 20% magnesium sulfate into a syringe and infuse via a syringe pump at 60ml/hr) to be administered by a doctor. |
| **Maintenance Dose** | 1 g/hr magnesium sulfate<br>(draw up 20% magnesium sulfate into a 50ml syringe and infuse via a syringe pump at 5ml/hour) |
| **Contraindications and cautions** | **Contraindication:** Acute renal failure.<br><br>**Caution:** Cardiac disease. |
| **Duration of infusion** | Continue infusion until delivery, or for a maximum of 24 hours if still undelivered. Review at 12 hours. It can then be discontinued EXCEPT in women who require ongoing infusion for severe pre-eclampsia/eclampsia who should be managed according to the pre-eclampsia guideline. |
| **Monitoring** | • Clinical:<br>– Patellar reflex (after completion of loading dose):<br>– Use arm reflexes in women with an epidural<br>– Strict in/out chart.<br>• ECG - Mandatory during and for one hour after loading dose<br>• Pulse oximetry - whilst infusion of magnesium sulfate in progress<br>***Presence of reflexes, $PO_2$ and urinary output <u>MUST</u> be recorded hourly on the high dependency chart *** |

## Appendix 2: Signs of magnesium sulfate toxicity

Experience from the Collaborative Eclampsia and Magpie Trials indicates that magnesium sulfate (according to the above regime) can be used safely without the need to monitor any levels. [3,6]

Magnesium is excreted by the kidneys and toxicity is more likely if there is oliguria (urine output less than 100 ml over 4 hrs) or urea greater than 10 mmol/L - halve the dose and check magnesium levels.

| **Signs of toxicity are extremely uncommon and correlate with magnesium levels:** | **Magnesium level (mmol/L)** |
|---|---|
| Loss of reflexes, weakness, nausea, feeling of warmth, flushing, somnolence, double vision, slurred speech | 5 |
| Muscle paralysis, respiratory arrest | 6-7.5 |
| Cardiac arrest | >12 |

| **Management of magnesium toxicity:** | |
|---|---|
| **Loss of patellar / biceps reflex** | 1. Stop maintenance infusion<br>2. Check magnesium level |
| **$PaO_2$ persistently <94%** | 1. Commence oxygen, check patellar reflex, inform Anaesthetist<br>2. If reflex present – exclude other causes (e.g. respiratory depression due to opiates or pulmonary oedema)<br>3. If reflex absent – see above |
| **Cardiorespiratory arrest** | 1. Stop maintenance infusion<br>2. Cardiopulmonary resuscitation<br>3. Administer 10 ml 10% calcium gluconate intravenously<br>4. Intubate immediately and manage with assisted ventilation until resumption of spontaneous respirations<br>5. if possible check magnesium level |

<u>If magnesium sulfate is being administered solely for fetal neuroprotection, in the absence of pre-eclampsia, it should be discontinued (and not restarted) if there are any signs of magnesium toxicity.</u>

If it needs to be restarted for severe pre-eclampsia, then follow the guidance in the severe pre-eclampsia guideline.