3Mg Clinical Guidelines Version 3, 10AUG2010

When patients present at the Emergency Department (ED) with acute severe asthma they may be eligible for the 3Mg Trial. Please keep the trial in mind and complete the Patient Recruitment Form for all acute severe asthma patients.

The aim of this trial is to measure the effectiveness of intravenous and nebulised magnesium sulphate in relieving symptoms of acute severe asthma and preventing hospital admission. The trial should determine whether magnesium sulphate should be standard first-line treatment for patients presenting to the ED with acute severe asthma.

We are not asking you to with-hold standard treatment from any patients. Standard treatment should be administered as detailed in the BTS/SIGN guidelines. The following protocol outlines the process of assessing patient eligibility, and the procedures to be completed if the patient is entered into the trial. It is split into two sections: Pre-randomisation and Post-randomisation. The full 3Mg protocol and more detailed guidance on each procedure can be found in the working file and site file.

Pre-Randomisation (Flow chart 1)

Please follow this section of the protocol for ALL patients presenting at the emergency department with acute severe asthma.

Immediate management

Make a rapid clinical assessment and attempt PEFR recording
Give urgent treatment according to BTS/SIGN guidelines:

- Commence salbutamol 5mg via oxygen-driven nebuliser or continue prehospital nebulisation
- Consider adding ipratropium 500mcg
- Give prednisolone 40-50mg orally or hydrocortisone 100-200mg IV

Assess for eligibility using the Patient Recruitment Form

- Take a patient pack from the working file (this contains all required paperwork)
- Complete the Patient Recruitment Form for all adults with acute severe asthma
- They must have features of severe asthma
- They must have NO life-threatening features
- They must have NO contraindication to magnesium sulphate
- They must not have received magnesium sulphate (IV or nebulised) in the previous 24 hours
- They cannot be a known previous participant in the 3Mg Trial

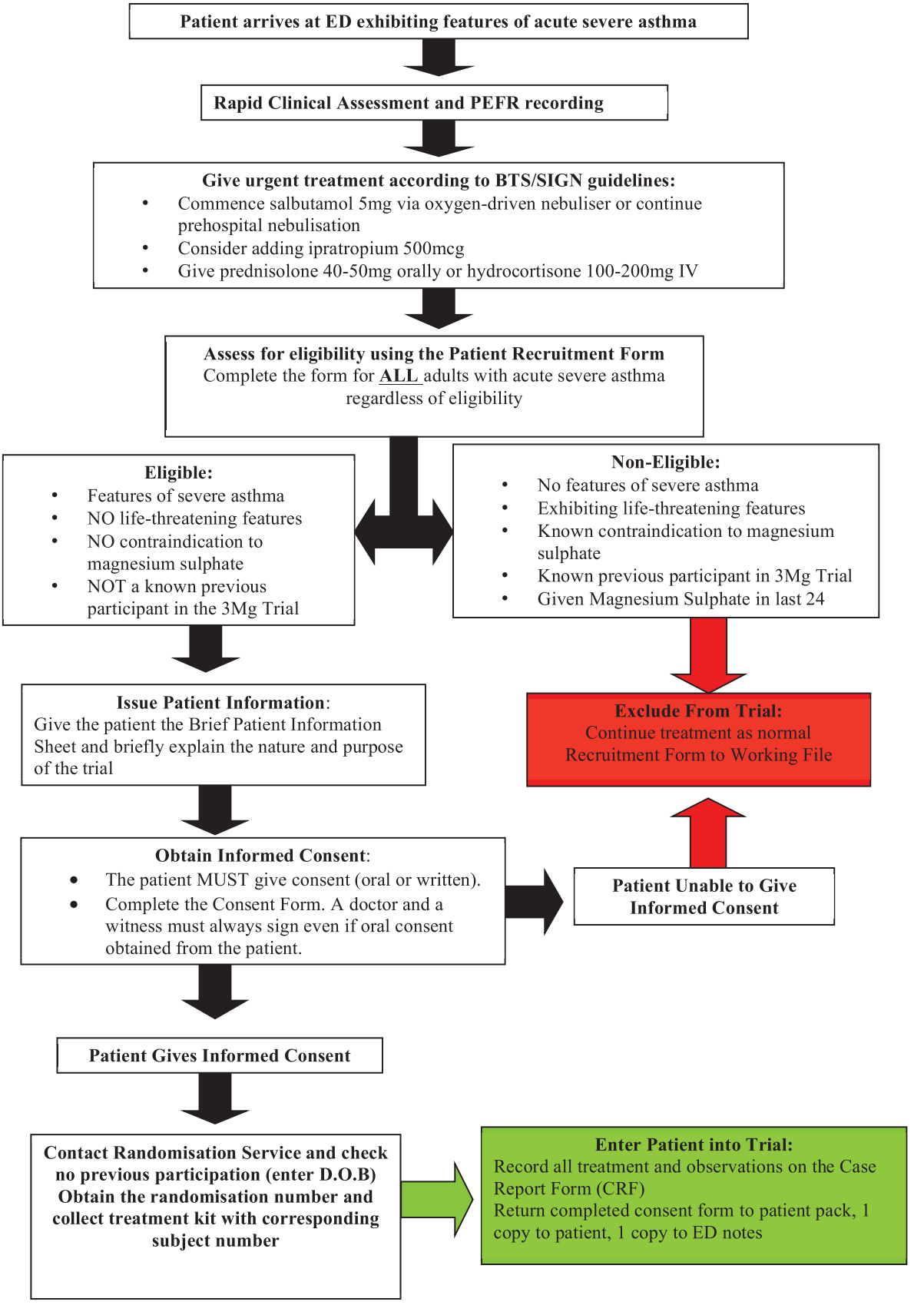
Information, consent and randomisation

- If eligible, give the patient the Brief Patient Information Sheet and briefly explain the nature and purpose of the trial
- Complete the first side of the randomisation form to check eligibility
- The patient MUST give consent (oral or written) before entry to the trial. Please complete the Consent Form and place original top copy in the patient pack. Give a copy of the consent form to the patient, and file a third copy in the ED notes.
- If the patient provides consent, contact the randomisation service (SIN and PIN printed in working file). Check for previous participation by entering D.O.B

on web system and then continue to obtain the treatment kit number. Complete the second side of the randomisation form and return it to the patient pack.

- If the patient is ineligible or does not give consent, only complete the front page of Patient Recruitment Form and file the in the non-recruited section of the working file. Add a blank Patient Recruitment Form to the patient pack and return it to the working file.

Flow Chart 1 – Pre-Randomisation to 3Mg Trial



Post-Randomisation (Flow Chart 2)

Please follow this section of the protocol for all patients who have been recruited into the trial.
Once participants have been randomised they immediately enter the trial and all details of treatment and any observations must be recorded on the case report form (CRF). However, participants are free to withdraw at any time, and the treatment can be unblinded if life-threatening features develop. If the patient withdraws or the treatment is unblinded, ensure this is recorded on page 4 of the CRF.

Baseline measurements
Record pulse, respiratory rate, blood pressure, temperature, oxygen saturation, oxygen flow rate, PEFR, and breathlessness VAS before starting treatment

Trial treatment
Participants are randomly allocated to one of three treatments. Treatment kits are labelled with a subject number (this is the same as randomisation number). Please ensure you use the correctly numbered kit. Before taking the kit from the cupboard, check the temperature log – if the temperature has exceeded 30ºC and a temperature excursion report has not been filed, you must not use until this has been done and the production unit have confirmed kits are safe to use (see temperature excursion section in working file).

Write a prescription (or use sticker if provided) of the 3Mg treatment kit in the patient notes, including the randomisation number and your signature:

3Mg IMP, randomisation number …..
- 1 x IV solution 100mls, over 20 mins
- 3 x nebulisers 7.5ml, started at 20 minute intervals

Each treatment kit contains one intravenous and three nebulised treatments, all of which must be used. Collapse the treatment kit box, write the patient initials and date on the box and place in the patient pack.
- Give the 100ml IV trial infusion over 20 minutes
- Give continuous trial nebulisers over at least one hour
- Record the total volume of trial treatment given on the Case Report Form

Nebulisation
- Continuous nebulisation should be provided using three consecutive nebulisers, each given over at least 20 minutes.
- For each nebuliser you should use one 7.5ml vial from the treatment kit.
- Up to 2.5ml of either 2.5mg or 5mg salbutamol, or saline can be added to each nebuliser, depending upon the patients' condition.
- Nebulisation should be driven by 6L/minute oxygen

Subsequent measurements
- Record the pulse, respiratory rate, blood pressure, oxygen saturation, oxygen flow rate, PEFR, and breathlessness VAS one hour and two hours after starting treatment

Concurrent and further management
- Patients should be reassessed frequently and the BTS/SIGN guidelines used to guide management

- Record any Adverse Events on the CRF and in ED notes and contact the PI as outlined in SAE reporting protocol.
- If the patient develops any life-threatening features or if their PEFR remains below 50% of best or predicted after trial treatment, then obtain arterial blood gases, chest X-ray and senior/ITU help. If appropriate, the trial treatment should be unblinded and intravenous magnesium sulphate considered.

Reassessment

- As soon as the patients' condition allows, give them the full Patient Information Sheet and ask them to complete the EQ-5D questionnaire (on the back of VAS scoring sheet). Place the completed questionnaire in the patient pack.
- If oral consent was given at entry to the trial, obtain written consent on a new consent form and place the completed consent form (original top copy) in the patient pack. Give a copy of the signed consent form for the patient to take home, and file another copy in the ED notes.

Admission or discharge

- Your decision to admit or discharge the patient should not be influenced by their participation in the trial.
- The patient should only be discharged home if, after a period of observation, they are stable and the PEFR is preferably above 75% (and definitely above 50%)
- The decision to admit or discharge can be made any time up to four hours after randomisation.
- If the decision has not been made by four hours, then the patient will be recorded as having been admitted to hospital.
- If the patient is admitted, please ensure that a ward admission letter (enclosed in patient pack) accompanies the patient to the ward so that staff are made aware of their participation in the trial.

Post-discharge care

- Prescribe steroids (BTS guidelines suggest prednisolone 40-50mg daily for 5 days)
- Ensure supply of inhaled beta agonist and steroid, and check inhaler technique
- Arrange GP follow-up
- Local research nurse will send GP letter

Trial paperwork

- Please complete the Case Report Form, especially any adverse events and side effects in the emergency department (page 4), and details of departure from the emergency department (page 3)
- Please put all paperwork in the patient pack and return to the Working File – ensure the EQ-5D questionnaire and VAS breathlessness scores have been completed
- Please ensure that the patient has a copy of both the brief and full Patient Information Sheet and a copy of their signed consent form

Thank you for recruiting a patient to the 3Mg Study.

Your local research nurse will have been alerted via the randomisation system and will visit the department in the next few days. The research nurse will complete the follow-up of the patient.

Flow Chart 2 – Post-randomisation to 3Mg Trial