SHARED CARE AGREEMENT

Use of Oromucosal Midazolam Maleate (Epistatus® 10mg in 1ml as an intervention for prolonged seizures and prevention of Status Epilepticus in children from 6 months to under 18 years of age.

Amber TLS – 1 Month

Principles of Shared Care

Shared care agreements provide a framework for the seamless transfer of care from a hospital or specialist service setting to general practice, where this is appropriate and, in the patient's, best interest. When a specialist considers a patient's condition to be stable or predictable, they may seek the agreement of the GP (or other primary care prescriber) concerned and the patient to share their care.

Patients and/or carers must be centrally involved in any decision-making process. They should be supported by good quality information that helps them to both come to an informed decision about engagement in a shared care arrangement and sets out the practical arrangements for ongoing supplies of medicines.

The existence of a shared care agreement does not necessarily mean that the GP has to agree to and accept clinical and legal responsibility for prescribing; they should only do so if they feel clinically confident in managing that condition. Clinical responsibility for prescribing is held by the person signing the prescription, who must also ensure adequate monitoring.

PLACE IN TREATMENT

Rectal Diazepam is another licensed product available for the treatment of status epilepticus, clusters of seizures and prolonged seizures (lasting 5 minutes or more) in children but using this route can be practically difficult and socially unacceptable. Oromucosal midazolam is as effective as rectal diazepam, is absorbed rapidly through the buccal cavity and has practical advantages of ease and social acceptability in administration.

The Epistatus® brand of oromucosal midazolam should only be initiated in new patients, or continued in existing patients, where there is a compelling reason to use this more concentrated solution. BUCCOLAM® has been the brand of choice for oromucosal midazolam on BSW Formulary since Nov 21. The 2.5mg/5mg/7.5mg/10mg are licensed for use in children from 3 months to < 18 years and the 10mg is also licensed for use in adults. Specialist nurses will review patients on Epistatus® and the aim will be to switch them to Buccolam®. Please prescribe by BRAND NAME.

If Buccolam® is unavailable, Epistatus® may be prescribed with caution and appropriate counselling. Epistatus® is a more concentrated solution. It is essential the dose of buccal midazolam prescribed on FP10 matches the dose in the syringe and the dose on the care plan before administering.

Responsibilities of Secondary Care Specialist (continued overleaf)

- Initiate treatment and prescribe the first supply of Epistatus® – this should be enough time to allow optimisation of treatment and demonstrate that the patient's response is consistent.
- It is the responsibility of the specialist to ensure that changes to prescription of oromucosal midazolam are clearly communicated in writing to the GP, family/carer and any other setting in which oromucosal midazolam is to be held for emergency use e.g. school nursing/pre-school teams.
- If a patient is switched to Buccolam® from Epistatus®, it is the responsibility of the specialist to arrange for corresponding care plans/administration plans to be updated accordingly and old supplies to be returned to the community pharmacy and replaced with the new prescription.
- Discuss the benefits and side effects of treatment with the patient and/or carers.
- Ensure that the patient/carer understands when and how to give the medication. An identified member of the specialist team such as epilepsy specialist nurse and community/school nurse, will work with the parents / carer to develop an Emergency Treatment Plan for child/young person with epilepsy for administration, train in use, ensure appropriate storage and provide written/verbal advice in a way that the individuals can understand.
- Review concurrent medications for potential interactions prior to initiation.
- Undertake the clinical assessment and relevant monitoring at baseline and during the initiation period.
- Communicate details of treatment to GP (in writing or via secure email) within the first month of treatment and ask the GP whether he or she is willing to participate in shared care.
- Discuss shared care arrangements with the patient/carer, obtain their consent and explain their responsibilities.

- Review the patient's condition and monitor response to treatment regularly where indicated (at least annually).
- Inform the GP after each clinic attendance if there is any change to treatment or monitoring.
- Supply the GP with background information about diagnosis, the reasons for selecting midazolam and details of how to prescribe it, including how often doses can be repeated, maximum dose in 24 hours and details of any combination therapy. This summary should be received within 14 days of a hospital outpatient review, in-patient stay or community review.
- Inform the appropriate community nursing service that oromucosal midazolam has been prescribed (by brand name). A Health Care Plan should be put into place by the appropriate community nursing service to support use.
- Ensure that clear arrangements exist for GPs to obtain advice and support.
- Report adverse events to the MHRA: https://yellowcard.mhra.gov.uk/
- Stop treatment where appropriate or provide GP with advice on when to stop.

Responsibilities of GP/Primary Care Prescriber

- Reply to the request as soon as practicable if they are **unable** to support shared care (in writing or via secure email).
- Prescribe Epistatus® after communication with specialist about need for treatment and the formulation to be used and the dose recommended.
- Midazolam is a schedule 3 controlled drug and therefore subject to the requirement for the quantity to be supplied to be written in words and figures and the dose to be on the prescription.
- Undertake ongoing clinical assessment and relevant monitoring following initiation period.
- Annual review and dosage adjustment required as dosage based on age (as advised by specialist nurse).
- Review any new concurrent medications for potential interactions.
- Refer promptly to specialist when any loss of clinical efficacy is suspected (e.g. worsening of disease-related symptoms, new symptoms suggestive of disease recurrence or progression) or intolerance to therapy occurs.
- Report to and seek advice from the specialist on any aspect of patient care that is of concern and may affect treatment.
- Stop treatment on the advice of the specialist.
- Report adverse events to the specialist and MHRA: https://yellowcard.mhra.gov.uk/

Responsibilities of Patient/Carer

- Report to the specialist, community nurse or GP if he or she does not have a clear understanding of the treatment.
- Share any concerns in relation to treatment with medicine. Please contact specialist if you start to need treatment more frequently.
- Report any adverse effects to the specialist, community nurse or GP whilst taking the medicine.
- Attend appointments for clinical review and monitoring.

1. Summary of condition and treatment aims Include links to relevant clinical guidelines e.g. NICE	Epilepsies in children, young people and adults NICE guideline NG217 (Published 27 April 2022): https://www.nice.org.uk/Guidance/ng217 • Only prescribe oromucosal midazolam for use in the community for children and young people who have had a previous episode of prolonged or serial convulsive seizures. • Over- and potentially inappropriate prescription of emergency benzodiazepines should not be used to alleviate individual, parental or carer's anxiety.	
2. Details of medicine and indication Please state whether licensed or unlicensed (off-label) use. Note that shared care is generally unsuitable for off-label prescribing unless it is a widely recognised use (e.g. included in BNF)	Treatment for children and young people with prolonged (lasting 5 minutes or more), repeated or cluster (typically three or more self-terminating seizures in 24 hours) generalised, convulsive (tonic–clonic, tonic or clonic) seizures in the community. To be used as per patient specific individual agreed protocol and care plan. Licensed for treatment of prolonged, acute, convulsive seizures in infants, toddlers, children and adolescents (from 3 – 6 months (hospital setting only) to < 18 years). Oromucosal midazolam is a short acting benzodiazepine that offers an alternative to rectal diazepam. Must only be used by parents/carers where the patient has been diagnosed with epilepsy.	
3. Pharmaceutical aspects	Route of administration:	Epistatus® is for oromucosal use

	Formulation:	Pre-filled needle-free oral syringe
	Administration details:	Please refer to SPC and PIL. Epistatus Oromucosal Solution
	Other important information:	**Not for intravenous use.** SAFETY: MHRA Guidance; The MHRA issued a warning (Drug Safety Update in October 2011) that care was needed if transferring between Epistatus® and Buccolam® due to the differences in strengths between the products. http://www.mhra.gov.uk/Safetyinformation/DrugSafetyUpdate/CON131931

4. Usual dose and frequency (including details of dose adjustments, e.g. in renal impairment) and duration of therapy

Transfer of monitoring and prescribing to Primary care is normally after the patient is on regular dose and with satisfactory investigation results.
All dose or formulation adjustments will be the responsibility of the initiating specialist unless directions have been discussed and agreed with the primary care clinician.
The duration of treatment will be determined by the specialist, based on clinical response and tolerability.
Termination of treatment will be the responsibility of the specialist.

Standard dosage:
Epistatus pre-filled oral syringes are available in four colour-coded doses and are prescribed according to the patient's age as follows:

Age range	Dose	Label colour
3 to 6 months hospital setting	2.5 mg	Yellow
> 6 months to < 1 year	2.5 mg	Yellow
1 year to < 5 years	5 mg	Blue
5 years to < 10 years	7.5 mg	Purple
10 years to < 18 years	10 mg	Orange

Epistatus® should be given by the oromucosal route (i.e. the area between the lower gums and inner cheek area of either side of the mouth). The full amount of the solution can be administered on one side but we generally recommend giving approximately half the dose on each side. This should be specified in the individual care plan.
The solution should be administered slowly into the space between the gum and the cheek, avoiding contact with the tongue.
Standard advice given to parents – if seizure is not settling 5 minutes after the first dose then call 999 for an ambulance.
Follow advice on individualised care plan. A second dose of midazolam can be given 10 minutes after the first dose but for most children this is only advised in the presence of ambulance crew or a hospital setting. Retain the empty syringe of Epistatus® to give to the healthcare professional. This will provide information on the dose received by the patient.
What to do if a seizure starts again: A second or repeat dose when seizures re-occur after an initial response should not be given without prior medical advice UNLESS its specified in their care plan.
Review and discontinuation of treatment
An ongoing review of the continued need for emergency rescue treatment with oromucosal midazolam should be carried out by **a specialist** at least every 12 months to ensure the seizure management plan is still appropriate and to prevent unnecessary long-term prescribing.

5. Baseline investigations and initial monitoring to be undertaken by specialist

Baseline investigations

- None required

6. Ongoing monitoring requirements to be undertaken by primary care

- None required

7. Action(s) to be taken by primary

- If frequency of use increases seek advice from the specialist team

care if abnormal result(s)	
8. Cautions and contraindications Please note this does not replace the Summary of Product Characteristics (SPC) and should be read in conjunction with it.	**Cautions** • Care must be taken when administering the product to avoid the risk of the patient choking. • *Respiratory insufficiency:* Midazolam should be used with caution in patients with chronic respiratory insufficiency because midazolam may further depress respiration. • *Altered elimination of midazolam:* Midazolam should be used with caution in patients with chronic renal failure, impaired hepatic or cardiac function. Midazolam may accumulate in patients with chronic renal failure or impaired hepatic function whilst in patients with impaired cardiac function it may cause decreased clearance of midazolam. • *Concomitant use with other benzodiazepines:* Debilitated patients are more prone to the central nervous system (CNS) effects of benzodiazepines. • *Risk from concomitant use of opioids:* Concomitant use of midazolam and opioids may result in sedation, respiratory depression, coma and death. Because of these risks, concomitant prescribing of sedative medicines such as benzodiazepines or related drugs such as midazolam with opioids should be reserved for patients for whom alternative treatment options are not possible. If a decision is made to prescribe midazolam concomitantly with opioids, the lowest effective dose and the shortest possible duration of opioids should be used. • The patients should be followed closely for signs and symptoms of respiratory depression and sedation. In this respect, it is strongly recommended to inform patients and their caregivers (where applicable) to be aware of these symptoms. • *Medical history of alcohol and drug abuse:* Midazolam should be avoided in patients with a medical history of alcohol or drug abuse. • *Amnesia:* Midazolam may cause anterograde amnesia. • *Excipients of known effect:* MALTITOL; Epistatus® contains maltitol. Patients with rare hereditary problems of fructose intolerance should not take this medicine. • ETHANOL; Epistatus® contains 197 mg ethanol in each mL which is equivalent to 25 vol%. The amount per mL is equivalent to less than 5 ml of beer or 2 mL wine. The small amount of alcohol in this medicine will not have any noticeable effects. **Contraindications** • Hypersensitivity to the active substance, benzodiazepines or to any of the excipients • Myasthenia gravis. • Severe respiratory insufficiency. • Sleep apnoea syndrome. • Severe hepatic impairment.
9. Significant medicine and food interactions and management For a comprehensive list, consult the BNF or Summary of Product Characteristics (SPC)	• Midazolam is metabolized by cytochrome P450 3A4 isozyme (CYP3A4). Inhibitors and inducers of CYP3A4 have the potential to respectively increase and decrease the plasma concentrations and, subsequently, the effects of midazolam thus requiring dose adjustments accordingly. • Calcium channel blockers, erythromycin, other macrolides, azole antifungals, cimetidine, ranitidine, omeprazole and grapefruit juice reduce the clearance of midazolam. This may result in prolonged duration of sedative effect. • Midazolam may interact with other hepatically metabolised medicinal products, e.g. phenytoin, causing potentiation.
10. Adverse effects and management Include details of incidence, identification, importance and management.	**Adverse Effects (see SPC for full list)** • The most common side effects with Epistatus® (seen in 1/100 to 1/10) are sedation, somnolence, depressed levels of consciousness, respiratory depression and nausea and vomiting. All patients receiving midazolam are likely to be drowsy for several hours after administration.

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- Respiratory depression occurs at a rate of up to 5%, although this is a known complication of convulsive seizures as well as being related to benzodiazepine use.
- Uncommonly/frequency not known; agitation, restlessness, confusion and disorientation have been reported.

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<tr><td>11. Advice to patients and carers
The specialist will counsel the patient with regard to the benefits and risks of treatment and will provide the patient with any relevant information and advice, including patient information leaflets on individual medicines.</td><td>
Epistatus pre-filled oral syringes are available in four colour-coded doses and are prescribed according to the patient's age as follows:
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</table>

Read Patient Information Leaflet carefully to understand how to give the medication.
Seek medical advice from your doctor, nurse or pharmacist if further enquiry required.
Keep the syringe to show to the ambulance staff or doctor after administration.
Do not store above 25°C. Do not refrigerate or freeze. Store in the original package to protect from light.

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<tr><td>12. Pregnancy and breast feeding
It is the responsibility of the specialist to provide advice on the need for contraception to male and female patients on initiation and at each review but the ongoing responsibility for providing this advice rests with both the GP and the specialist.</td><td>
Pregnancy:

There are no or limited amount of data from the use of midazolam in pregnant women.
Midazolam may be used during pregnancy if clearly necessary. The risk for new-born infants should be taken into account in the event of administration of midazolam in the third trimester of pregnancy.

Breastfeeding:

Midazolam is excreted in low quantities (0.6%) in human milk. As a result, it may not be necessary to stop breast feeding following a single dose of midazolam.

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<tr><td>13. Specialist contact information</td><td>
<table>
<tr><td>Contact details</td><td>Telephone no.</td><td>Email address</td></tr>
<tr><td>Faye Price
RUH Paediatric Epilepsy Nurse Specialist</td><td>01225 825375</td><td>Faye.price@nhs.net</td></tr>
<tr><td>Salisbury District Hospital Epilepsy Nurse Specialist</td><td>01722 336 262</td><td>sft.paedsepilepsy@nhs.net</td></tr>
<tr><td>Susan Mulhall & Natasha Thomas
GWH paediatric Epilepsy Nurse Specialists</td><td>01793 604969
(24 hour voicemail)</td><td>susan.mulhall@nhs.net
Natasha.thomas22@nhs.net</td></tr>
<tr><td colspan="3">Other Specialist Contact Information</td></tr>
<tr><td colspan="3"></td></tr>
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<tr><td>14. Additional information</td><td></td></tr>
<tr><td>15. References</td><td>

- Summary of Product Characteristics for Epistatus® via https://www.medicines.org.uk/emc/search?q=epistatus
- BNFC online via https://bnfc.nice.org.uk/
- Epilepsies in children, young people and adults NICE NG217 (Published 27 April 2022): https://www.nice.org.uk/guidance/ng217

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<tr><td>16. To be read in conjunction with the following documents</td><td>

- NHS England: Responsibility for Prescribing Between Primary & Secondary/ Tertiary Care. Ref 07573, Version 1.0, Published January 2018. Accessed via: https://www.england.nhs.uk/publication/responsibility-for-prescribing-between-primary-and-secondary-tertiary-care/ Click or tap here to enter text.

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Date Last Updated:	Earlier versions of Epistatus SCA for children [use in <10yrs (unlic) and >10yrs (licensed)] approved 18/11/21. Jan 2023 update incorporates changes in Epistatus licence and links to updated NICE guidance. Updated February 2025 to include adult licenses.
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