

Shared Care Guidelines: Use of oromucosal midazolam as an intervention for prolonged seizures and prevention of Status Epilepticus in adolescents (**≥10 years**) and adults. (TLS amber) (Epistatus® 10mg in 1ml pre-filled syringe)

PLEASE NOTE: Epistatus is the brand of choice in NHS BaNES/NHS Swindon/NHS Wiltshire. Prescribe by BRAND NAME. Community nurses can only provide training on the use of this brand in carer & school settings. ALL patients should now be prescribed pre-filled syringes and should NOT receive the multi-dose bottle.

AREAS OF RESPONSIBILITY FOR THE SHARING OF CARE

This shared care agreement outlines ways in which the responsibilities for managing the prescribing of midazolam for adult & adolescent patients prone to prolonged generalised seizures (lasting longer than 5 minutes), clusters of seizures or status epilepticus can be shared between the specialist and the general practitioner (GP). GPs are invited to participate but if the GP is not confident to undertake these roles, they are under no obligation to do so. In such an event, the clinical responsibility for the patient in respect of this diagnosed condition remains with the specialist. **If a specialist asks the GP to prescribe this drug, the GP should reply to this request as soon as practicable.**

Sharing of care assumes communication between the specialist, GP, patient and their carers. The intention to share care should be explained to the patient and their carers by the specialist initiating treatment.

Epistatus® is indicated for the treatment of prolonged, acute, convulsive seizures in children and adolescents aged 10 to less than 18 years. Please note that Epistatus® currently does not have a license for use in children under the age of 10 years of age or in adults. Please see the separate shared care agreement for use of Epistatus in children <10 years of age on the formulary websites if your patient is under 10 years of age. The manufacturers are currently pursuing a license for this age group as well as in adults. There are currently no buccal midazolam products that are licensed to be used in adults.

The doctor or nurse who prescribes the medication legally assumes clinical responsibility for the drug and the consequences of its use.

PLACE IN TREATMENT

Rectal Diazepam is another licensed product available to adults for the treatment of status epilepticus, clusters of seizures and prolonged seizures but using this route can be practically difficult and socially unacceptable.

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.

Midazolam oromucosal solution is available as:

Epistatus® - containing **midazolam maleate 10mg in 1mL**.

Prefilled Oral Syringes :

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|---|---|
| <p>2.5mg / 0.25ml
5mg / 0.5ml
7.5mg / 0.75ml
10mg / 1ml</p> | <p>UNLICENSED. For use in children under 10 years of age.
Individually wrapped pre-filled oral syringes (pack of 4)</p> |
| | <p>LICENSED product for children aged 10 to less than 18 years of age. Available as a single pre-filled syringe.</p> |

Bottle: UNLICENSED. 5-ml multi dose bottle with four oral syringes in the packaging. Any patients already using this should be moved from this format to the licensed pre-filled 10mg in 1ml syringe.

▼ **Buccolam®** - a licensed preparation for children containing **midazolam hydrochloride 5mg in 1mL (note the different strength)** in pre-filled oral syringes of 2.5mg, 5mg, 7.5mg and 10mg. ▼ **Buccolam® is NOT currently included in local formularies and so should not be prescribed.**

The consensus view of local specialists is to continue to use the Epistatus® as the product of choice at the current time. (July 2017)

KEY MESSAGES

- **Epistatus®** (unlicensed brand currently recommended) is **TWICE** the strength of ▼ **Buccolam®**
- Midazolam oromucosal solution should be **prescribed by brand name**; if this is not prescribed by brand name, pharmacists should check the intended product with prescribers.
- Care is required to ensure that patients and carers receive the product they are expecting and are familiar with.

RESPONSIBILITIES and ROLES

Specialist responsibilities	
1	Initiate treatment and provide at least 2 doses of 10mg/ml x 1ml prefilled syringes.
2	Discuss the benefits and side effects of treatment with the patient. The prescriber must make every effort to obtain consent to treatment and inform the patient and carer of the medicine's license status (if ≥18 yrs).
3	Ensure that the patient/carer understands when and how to give the medication (For adolescents, an identified member of the Children and Young People's Training Team, epilepsy specialist nurse or Public Health School Nurse (PHSN), will work with the patient and carer to develop an Epilepsy Emergency Plan for administration, train in use, ensure appropriate storage and provide written/verbal advice in a way that the individuals can understand (as per Joint Epilepsy Council Guideline 2012)
4	Ask the GP whether they are willing to participate in shared care. The GP must be informed of the medicine's license status if it is for an adult.
5	Supply the GP with background information about diagnosis, the reasons for selecting midazolam and details of how to prescribe it, including details of 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.
6	Inform the appropriate community service that Buccal Midazolam has been prescribed. A Health Care Plan/Flow Chart should be put into place by the appropriate community service to support use.
7	Review the patient's condition and monitor response to treatment regularly (at least 6 monthly).
8	Advise GP on when to stop, alter or change treatment.
9	Report adverse events to the MHRA https://yellowcard.mhra.gov.uk/
10	Ensure clear arrangements for GP and carer back-up, advice and support

General Practitioner responsibilities	
1	Reply to the request for shared care as soon as practicable.
2	Prescribe midazolam after communication with specialist about need for treatment and the formulation to be used and the dose recommended.
3	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.
4	Refer promptly to specialist if frequency of use increases, lack of clinical efficacy is suspected or any concerns arise.
5	Report to and seek advice from specialist on any aspect of patient care that is of concern to the GP and may affect Treatment.
6	Stop treatment on the advice of the specialist.
7	Report adverse events to the specialist and MHRA https://yellowcard.mhra.gov.uk/

Community Pharmacist's role	
1	If the prescription is written generically confirm with the patient &/or GP as to which brand the patient uses (should be Epistatus). Endeavour to get the GP practice to change the patient's records to the correct brand.
2	The licensed Epistatus 10mg in 1ml syringe should be used for the 10 to under 18 age group (& off-label for adults). If a different product such as a special has been prescribed, contact the prescriber to get the prescription changed to the licensed product of local choice (Epistatus).
3	Ensure that each Epistatus 10mg in 1ml pre-filled syringe (PFS) is labelled on the outside of the box it comes in. Usually, 1 or 2 PFS will be supplied for each patient at a time.
3	Check that the patient/carer collecting the prescription understands how to use it.

Patient's role	
1	Report to the specialist or GP if he or she does not have a clear understanding of the treatment.
2	Share any concerns in relation to treatment with medicine.
3	Report any adverse effects to the specialist or GP whilst taking the medicine.

Epilepsies: diagnosis and management NICE CG137 (Updated February 2016): <https://www.nice.org.uk/Guidance/cg137>

- Only prescribe buccal midazolam for use in the community for children, young people and adults who have had a previous episode of prolonged or serial convulsive seizures
- Over- and potentially inappropriate prescription of emergency benzodiazepines should not be used as a means to alleviate individual, parental or carer's anxiety.

Review and discontinuation of treatment

- An ongoing review of the continued need for emergency rescue treatment with buccal midazolam should be carried out by a **specialist** at least every 6 months to ensure the seizure management plan is still appropriate and to prevent unnecessary long term prescribing.
- Midazolam may be withdrawn if the patient has been fit free over a 2 year period.

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>

There have also been other errors reported to the National and Reporting Learning System (NRLS) involving confusion between the mg and mL eg 2.5mL (25mg) was prescribed when 0.25mL (2.5mg) was intended.

<http://www.nrls.npsa.nhs.uk/resources/type/signals/?entryid45=132975>

MEDICATION DETAILS

Indication	Prolonged, acute, convulsive seizures. Midazolam is a short acting benzodiazepine that offers an alternative to rectal diazepam
Products available	Epistatus® - pre-filled syringe containing midazolam maleate 10mg in 1mL . Licensed for age 10 to under 18s. Also product of choice in adults (off-label).
Form	Pre-filled oral syringe 10mg in 1ml
Administration	Using the prefilled syringe: half the contents should be squirted into each buccal cavity.
Dose and frequency	Dose for children over 10 years and adults: 10mg (1ml) Carers should only administer a single dose of midazolam. If the seizure has not stopped within 10 minutes after administration of midazolam, emergency medical assistance must be sought and the empty syringe given to the healthcare professional to provide information on the dose and product received by the patient. A second dose can be given ONLY if assessed as necessary and stated on the emergency epilepsy plan) this is assessed on an individual basis and will be clearly stated in the Epilepsy Emergency Plan. The second dose is usually given 10 minutes after the first dose. If the patients' breathing becomes shallow, call an ambulance and do not administer a second dose. If a response is not seen 5 minutes after a second dose, call 999 for an ambulance What to do if a seizure starts again: The official guidance states that no more doses should be given in the next 12 hours for bigger children and adults. Each individual epilepsy emergency plan will state when an ambulance should be called with regard to the management of ongoing seizures. The maximum recommended adult dose in 24 hours is 20mg . Please follow the advice given by the initiating specialist.
Contra- indications	Hypersensitivity to the active substance (midazolam), benzodiazepines or to any of the excipients Myasthenia gravis. Severe respiratory insufficiency. Sleep apnoea syndrome. Severe hepatic impairment.
Cautions	Midazolam should be used with caution in patients with chronic respiratory insufficiency because midazolam may further depress respiration. 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. Debilitated patients are more prone to the central nervous system (CNS) effects of benzodiazepines and, therefore, lower doses may be required. Midazolam should be avoided in patients with a medical history of alcohol or drug abuse. Midazolam may cause anterograde amnesia.
Side effects	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 Rare: agitation, restlessness and disorientation have been reported. See SPC for full details: http://www.medicines.org.uk/emc/medicine/33476
Monitoring	No specific monitoring is necessary
Drug interactions	Calcium channel blockers, erythromycin, other macrolides and cimetidine reduce the clearance of midazolam. This may result in prolonged duration of sedative effect. See SPC for full details: http://www.medicines.org.uk/emc/medicine/33476
Storage	Do not store above 25°C. Do not store in a fridge as crystallisation may occur.

BACK-UP ADVICE AND SUPPORT

Contact details	Telephone No.	Bleep:	Fax:	Email address:
Carole Leslie Epilepsy Specialist Nurse (Learning Disabilities) Complex Health Needs Service ASH House St Martin's Hospital Clara Cross Lane Bath BA2 5RP	Tel 01225 831566			Carole.Leslie@sirona-cic.org.uk <hr/> <hr/>
<u>RUH Hospital Pharmacy Dept:</u> Pharmacy dispensary (for prescription queries) Pharmacy out-patients	01225 824640 01225 825869			
Lou Pitman Lead Pharmacist for Family Services Pharmacy Department Salisbury District Hospital Odstock Rd Salisbury SP2 8BJ	01722 336 262 (Bleep 3134)			louisepitman@nhs.net
Dr Joanna Lovett, Consultant Neurologist Salisbury District Hospital and Wessex Neurological Centre, Southampton General Hospital	01722 336 262 x4233			Joanna.Lovett@salisbury.nhs.uk
Community Paediatrics, Wiltshire Community Children's Service Derby Court, White horse Business Park, Trowbridge, BA14 OXG	0333 321 0021			VCL.childhealthadmin@nhs.net
<u>GWH adult epilepsy nurse specialists:</u> Leah Baigel Bridget Borland <u>GWH Consultant neurologist (adults):</u> Dr Stephan Hinze	01793-605946			leah.baigel@gwh.nhs.uk Bridget.Borland@gwh.nhs.uk stephan.hinze@gwh.nhs.uk
<u>GWH paediatric epilepsy specialist nurse:</u> Susan Mulhall <u>GWH paediatric specialist pharmacist:</u> Cathy Dewdney	01793 604969 (24 hour voicemail) 01793 605193	- 1327		susan.mulhall@nhs.net Cathy.Dewdney@gwh.nhs.uk

References

- Drug Tariff http://www.ppa.org.uk/ppa/edt_intro.htm
- Epilepsy Action <https://www.epilepsy.org.uk/>
- Epilepsy Society <http://www.epilepsysociety.org.uk/>
- Joint Epilepsy Council <http://www.jointepilepsycouncil.org.uk/>
- NICE Guidance, The Epilepsies <http://www.nice.org.uk/Guidance/cg137> (last updated Feb 2016)
- Young Epilepsy <http://www.youngpilepsy.org.uk/about-us/>