Buccal Midazolam Guidelines

Introduction:

Buccal Midazolam has been approved by NICE (2012) as a first line drug in children and young adults who develop prolonged convulsive seizures (Ref. 1). Buccal Midazolam has been proven equally effective to rectal diazepam in comparative studies (ref. 2, 3). It is convenient and socially acceptable for children of all ages. Side effect (such as respiratory depression) profile is similar to rectal diazepam. EPEN recommends its use as first line drug in prolonged convulsive seizures and developed the following guidelines.

Indications:

- Prolonged febrile convulsions
- Prolonged afebrile convulsive seizures
- Prolonged non-convulsive epileptic seizures on advise by paediatric neurologist or paediatrician with expertise in epilepsy
- Cluster of seizures after stipulated time, upon discussion and recommendation by paediatrician with expertise in epilepsy or paediatric neurologist
- Consider re-introduction (including care plan) while weaning anticonvulsants in those children who suffered from refractory epilepsy with prolonged seizures in the past.

Contraindications:

- Hypersensitivity to the active substance, benzodiazepines or to any of the excipients
- Myasthenia gravis
- Severe respiratory insufficiency
- Severe hepatic impairment

Warnings or precautions:

Use Buccal Midazolam with care in following situations

- Chronic lung disease
- Chronic renal failure
- Liver dysfunction
- Sleep apnoea syndrome
- Concomitant use of other benzodiazepines (e.g. Clobazam, Clonazepam, Diazepam)

Who can prescribe?

Prescription can be recommended by paediatrician, paediatric neurologist or epilepsy specialist nurse. First and follow up prescriptions should be made by a qualified prescriber (Doctor including GP or nurse specialist who is a qualified prescriber).

Who can administer?

Parents, carers or professionals, who have received training in administration of Buccal Midazolam.

Time of administration:

Generally it is recommended to administer after **5 minutes** of the onset of a convulsive seizure. However in some individual children or in children with refractory seizures, this time of intervention could be altered. This should be agreed and documented by professionals involved in the care plan.

Doses:

As per BNFc (ref. 4)

Child up to 6 months: 0.3mg/kg, max 2.5mg.
6months to -1 years: 2.5mg
1-5 years: 5mg
5-10 years: 7.5mg
>10 years: 10mg

Always prescribe in milligrams, but also train parents in millilitres

Route: Buccal

Preparations:

Brand	Company	Chemical Product	Preparation	Strength	License Status
Buccolam	ViroPharma	Midazolam Hydrochloride	Prefilled syringes	2.5, 5, 7.5 and 10mg Syringes	Licensed for 3mo to 18 yrs
Epistatus	Special Products	Midazolam Maleate	Oral solution 5ml	10mg/1ml	Unlicensed in Children
Epistatus	Special products	Midazolam Maleate	Prefilled syringes	2.5, 5, 7.5 and 10mg Syringes	Unlicensed in Children
Rosalam	Rosemont	Midazolam Hydrochloride	Oral solution 5ml	10mg/1ml	Unlicensed
Buccal Midazolam (generic)	Quantum and Martindale	Midazolam Hydrochloride	Oral solution 5ml	10mg/1ml	Unlicensed
EPI-CALM	?	Midazolam Hydrochloride	Multi-doe bottle	10mg/1ml	Unlicensed

Parents should be made aware of licensed status of preparations. It is recommended that licensed preparation is prescribed in preference to unlicensed one. If an unlicensed preparation is prescribed it should be discussed with parents and choice should be documented. Efficacy may vary between Midazolam hydrochloride and maleate preparations.

Information to parents:

Leaflet of information on Midazolam can be obtained from medicines for children web site (ref. 5)

Side Effects:

Common (affect between 1 in 10 and 1 in 100 people): Sedation, reduced levels of consciousness, nausea or vomiting, slow and shallow breathing.
Uncommon (affect between 1 in 100 and 1 in 1000 people): Rash, itchy skin and hives.
Very rare (affect less than 1 in 10,000 people): Aggression or anger, agitation, confusion, hallucinations, temporary memory loss, dizziness, headache and respiratory depression (ref. 7). Expert group discussion, Excel 2012 concluded that respiratory depression was extremely unlikely after 20 minutes following administration.

Training:

Parents and carers should be provided with training of administration of Buccal Midazolam. Training is provided by specialist nurses or other health professionals trained in this field. Parents should be provided with leaflets containing illustrations of procedural administration. Alternatively parents may watch the video. Leaflets of administration can be downloaded from EPEN website (ref. 6). If there is high chance of occurrence of convulsive seizure in school, it is recommended to train the school staff. Individual circumstances (e.g. geographical access to ambulance or refractory seizures) should be carefully considered in training many carers.

Retraining should take place when discontinued midazolam is reinstituted.

Seizure Care Plan:

It is always recommended that children who have been prescribed with Buccal Midazolam should have a seizure care plan prepared and distributed to all users in the community. Copies should be kept with parents and school.

Caution on first dose administration:

Ideally first dose should be given in the presence of a trained health care professional, who can deal with medical emergencies (e.g. Paramedics or in-hospital). However in emergency situations, where ambulance access is remote, call paramedics immediately and medicine can be given. Test doses are not normally required as the risk of apnoea is extremely low (Excel 2012).

Repeat doses:

EPEN does not recommend a second dose in 12 hour after first dose. In some specific cases (who have repeated episodes of status unresponsive to single dose), a 2nd dose can be used if the first dose is ineffective. However, this should be considered on an individual basis by the treating physician in-charge. It should be documented in the care plan. Repeat dose can be of same or reduced dose. It is advised to administer the second dose on arrival of paramedic if practical.

Caution with other benzodiazepines:

Caution should be exercised with further drugs in this group in case of treatment of status epilepticus. In any situation, it is recommended that no more than 2 doses of benzodiazepines should be given in the treatment of status epilepticus.

Compatibility with Ketogenic Diet:

There is no carbohydrate in any of the preparations therefore Midazolam is suitable for patients receiving ketogenic diet.

Storage:
Store at room temperature (not in refrigerator) away from bright light or heat.

Review of prescription:

Need for continuation of prescription should be reviewed annually. If Buccal Midazolam is not used for 12 months, it is recommended to stop further prescriptions. However this practice may vary in individual case on clinician's discretion.

References:

1. The epilepsies: the diagnosis and management of the epilepsies in adults and children in primary and secondary care. NICE Clinical guideline, CG 137, Issued January 2012**.**
2. Safety and efficacy of Buccal Midazolam versus rectal diazepam for emergency treatment of seizures in children: a randomised controlled trial. McIntyre J, Robertson S, Norris E, Appleton R, Whitehouse WP, Phillips B, Martland T, Berry K, Collier J, Smith S, Choonara I. *The Lancet*. 2005 July; 366(9481):205-10.
3. Buccal midazolam and rectal diazepam for treatment of prolonged seizures in childhood and adolescence: a randomised trial. Scott RC, Besag FM, Neville BG. *The Lancet.* 1999 Feb 20;353(9153):623-6
4. BNF for children 2011-2012; Section 4.8.2 Drugs used in status epilepticus
5. http://www.medicinesforchildren.org.uk/search-for-a-leaflet/midazolam-for-stopping-seizures/
6. http://www.networks.nhs.uk/nhs-networks/eastern-paediatric-epilepsy-network/information-leaflets/midaz_leaflet_with_photos_logo.pdf/view.
7. Patient/User Information Leaflet; PIL.25527.1(1).pdf. Downloaded from Electronic Medicines Compendium: http://www.medicines.org.uk/EMC/medicine/25527/PIL/BUCCOLAM

Prepared by

Dr Tekki Rao, Dr V Gandhi, Mrs Liz Stevens (Luton), Dr Deepa Krishnakumar, Dr Alasdair Parker, Mrs Karen Higgins, Ms Sian Raymond (Addenbrookes, Cambridge), Ms Liz Hillier (Bedford) and Ms Sally Taylor (Norwich)

Developed and ratified: October 2012; Due for next review: October 2015