Bournemouth, Dorset and Poole Health Technologies Forum
Children's Epilepsy Service at Poole NHS Foundation Trust & Dorset County Hospitals

SHARED CARE GUIDELINES FOR PRESCRIBING BUCCAL MIDAZOLAM (BUCCOLAM®) IN CHILDREN

INDICATION

The administration of buccal midazolam for the control of prolonged, continuous or cluster of seizures is recognized as an effective treatment. This has resulted in its inclusion in the National Institute for Health and Clinical Excellence (NICE) clinical practice guideline on the diagnosis and management of epilepsy in children and adults published in October 2004 (CG 20) and January 2012 (CG 137).
The administration of buccal midazolam is considered to be a less invasive procedure than the administration of rectal diazepam and the issues of privacy and dignity are less compromised.

Buccal midazolam is now licensed for use in children from 3 months up until their 18th birthday. The licensed preparation is Buccolam® (midazolam hydrochloride 5mg/ml) available in 4 different sized pre-filled syringes to match the 4 doses used in children.
This preparation should be used for all newly diagnosed patients where there is a history of prolonged, frequent seizures[4].

Epistatus® (midazolam maleate 10mg/ml) is still an unlicensed product in the UK for all ages. Existing patients will continue to use this until they are reviewed in out-patient clinics (or as part of a related in-patient admission). When they, their parents and/or carers have received training to use Buccolam® syringes and have a new individual care plan in place, the Specialist will provide initial supply of Buccolam® and follow the steps below to communicate this change to their GP.

In this document, 'a Specialist' is defined as a Consultant Paediatrician with a special interest in Epilepsy, or a Consultant Paediatric Neurologist.

AREAS OF RESPONSIBILITY FOR SHARED CARE

This shared care agreement outlines suggested ways in which the responsibilities for managing the prescribing of buccal midazolam (Buccolam®) can be shared between the specialist and general practitioner (GP). GPs are expected to participate.

Training and support are available from the Children's Epilepsy Service at Poole Hospital NHS Foundation Trust for patient's seen in Poole clinics, and will be available from 1st November 2012 at Dorset County Hospital for patient's seen in clinics there, to help GPs who wish to participate but feel that they need up-dating in order to do so.
Under exceptional circumstances, if the GP is not confident to undertake these roles, then he or she is under no obligation to do so. In such an event, the total clinical responsibility for the patient for the 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 and patient, parents and/or carers. The intention to share care is usually explained to the patient and family by the doctor initiating treatment. It is important that patients and their families are consulted about treatment and are in agreement with it.

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

Specialist Responsibilities	
1	To assess the patient and establish the diagnosis, determine a management strategy and ensure appropriate follow-up in conjunction with the GP.
2	To ensure the patient and parents or carers have an individual care plan and have received training on the administration of Buccolam® in accordance with Joint Epilepsy Council (JEC) guidelines
3	To only recommend the use of buccal midazolam when the benefits outweigh the risks. These benefits and any side effects will be discussed with the patient and the parents or carers by the specialist
4	Once individual care plan and training are in place, to initiate treatment and provide an initial supply of at least 2 doses of Buccolam® in pre-filled syringes.
5	If possible, it is recommended that the first dose of buccal midazolam is administered in hospital, particularly for patients with a medical history of respiratory problems or previous adverse reaction to benzodiazepines. If this is not possible, then it is advisable that an ambulance is called the first time midazolam is given.
6	To provide the GP with appropriate prescribing information including background information about diagnosis, the reasons for selecting Buccolam®, details of how to prescribe it (including CD requirements), including details of how often doses can be repeated, maximum dose in 24 hours, whether the dose is administered in full on one side of the mouth or in two approximate halves on both sides of the mouth and details of any combination therapy and any additional information requested.
7	To provide the above information in a written care plan which is agreed with and signed by the parents and/or carers.
8	To be available for advice if the patient's condition changes.
9	To make every attempt to obtain consent to treatment. All information will be presented in a way that the individual/ parents/ carers can understand.
10	To liaise with the GP on any suggested changes in prescribed therapy.
11	The need for buccal midazolam can be reviewed at clinic appointments if not used for 12 months or more. If use to continue, the current dose should be reviewed according to their current age to determine if it is still appropriate. If the dose is changed, the care plan should be amended accordingly and sent to GP.

General Practitioner Responsibilities	
1	Reply to the request for shared care as soon as practicable
2	Prescribe Buccolam® pre-filled syringes after communication with the specialist about the need for treatment. It is recommended that prescriptions are maintained as acute prescriptions in the patient's medication record.
3	Refer promptly to the specialist if frequency of use increases, lack of clinical efficacy is suspected or any concerns arise
4	Report adverse events to specialist and CSM
5	Report and seek advice from specialist on any aspect of patient care that is of concern to the GP and may effect treatment
6	To continue prescribing Buccolam® until informed otherwise by the specialist
7	Stop, alter or change the treatment on advice of the specialist

Parents and/or Carers Responsibilities	
1	Attend training on epilepsy and the administration of Buccolam® pre-filled syringes provided by The Children's Epilepsy Service at Poole Hospital NHS Foundation Trust or Dorset County Hospital
2	Participate in developing an individualised care plan for the child with the specialist
3	To keep a record of when Buccolam® is given alongside a seizure diary or equivalent
4	Report to the specialist or GP if he or she does not have a clear understanding of the

	treatment.
5	Attend all the follow-up appointments with the Epilepsy Specialist and their GP
6	Share any concerns in relation to the treatment with buccal midazolam
7	Follow written care pathway agreed with Epilepsy Specialist and use written and other information on the medication.
8	Seek help urgently if suspect adverse effects, or otherwise unwell.

SUPPORTING INFORMATION

Before prescribing Buccal Midazolam (Buccolam®), the patient and their family should be informed that it is a controlled drug.

Training

Only individuals who have been directly trained by a professional authorized to provide training by the Children's Epilepsy Services at Poole Hospital NHS Foundation Trust or Dorset County Hospital, are allowed to administer Buccolam®.

There are a number of nurses in the paediatric department at both Poole Hospital NHS Foundation Trust and will be at Dorset County hospital from 1st Nov. 2012, who are trained to delivery buccal midazolam using Buccolam®. The training is provided in accordance with the manufacturer's instructions and the Joint Epilepsy Council (JEC) guidelines.

Children's Community Nurses and some special school nurses will also be trained to ensure availability of trained staff in the community setting. Training can be arranged through the Children's Epilepsy Clinics or the Community Paediatric Nursing teams.

Use of Buccolam® within Organisational settings (eg school, care homes)

- It is the individual organisation's responsibility to produce a statement regarding liability insurance to the effect that it covers staff carrying out the procedure
- Only individuals who have been directly trained by a professional authorized to provide training by the Children's Epilepsy Services, are allowed to administer Buccolam®.
- This training should not be cascaded to fellow staff
- At all times, staff and carers should be required to act within the guidelines of the individual care plan. Acting outside these guidelines carries personal responsibilities. Staff and carers will be made aware of this during training.

The Individual care plan

The detailed individual care plan is a confidential document which will be agreed with the parents and/or carers and signed by them. It will include the following:

- Detailed demographic patient information including full name, Date of birth, address, hospital number and NHS number
- Detailed seizure classification and description, including which seizures should be treated with Buccolam®.
- Possible seizure triggers
- Usual duration of seizure and normal recovery from seizure
- Contraindications (if any)

- Dose (in milligrams and milliliters) of Buccolam® to be given buccally, appropriate to the child's age
- Usual reaction to buccal midazolam
- Named person / people authorised to carry out this procedure
- If appropriate, who should witness the administration procedure
- Important side effects to look for
- **If** and when a second dose can be given (it should be noted that there is an increasing risk of respiratory depression when more than two doses of a benzodiazepine are administered)
- Maximum dose in 24 hours
- When emergency assistance (dial 999) should be sought
- Who should be informed eg parents and/or carers
- A record of the use of buccal midazolam, which should be up-dated after each administration

Dosage and Administration for Infants, Toddlers, Children and Adolescents (from 3 months to < 18 years of age):

Most epileptic seizures stop within 5 minutes. Since midazolam causes severe drowsiness and respiratory depression, administration should be delayed for 5 minutes to avoid giving it unnecessarily.
However, if it is known that the seizure always lasts for more than 5 minutes for an individual patient, then the specialist may advise that midazolam should be administered as soon as possible. This will be documented in the individual's care plan.

Buccolam® pre-filled syringes are colour-coded according to the dose contained within the syringe.
Standard doses are according to patient age as follows:

Age range	**Dose**	**Label colour**
3 to 6 months **hospital setting only**	2.5mg	Yellow
> 6 months to < 1 year	2.5mg	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

For infants between 3 to 6 months of age, treatment should always be within a hospital setting where monitoring is possible and resuscitation equipment is available[6].

Buccolam® should be given by the oromucosal route (ie 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 on the individual

care plan. The solution should be administered slowly into the space between the gum and the cheek, avoiding contact with the tongue, and the cheek pressed and massaged immediately to retain the solution and assist with absorption.

The first effects of midazolam are generally seen after approximately 5 minutes and the seizure controlled within 10 minutes. Parents and/or carers should only administer a single dose of medication.
If the seizure has not stopped within 10 minutes after administration of the midazolam, emergency medical assistance must be sought by dialing '999'. Parents and/or carers should continue to monitor breathing closely while waiting for the ambulance to arrive. The empty syringe should be given to the healthcare professional to provide information on the dose received by the patient.

When seizures recur after an initial response, a second or repeat dose should not be given without prior medical advice.
Under exceptional circumstances, a Specialist can agree with the parents and/or carers the use of a second dose of buccal midazolam. This will be documented in the individual's care plan.

Drowsiness will be observed for several hours after administration.

Contraindications and precautions

Contraindications include hypersensitivity to the active substance, benzodiazepines or any of the excipients (sodium chloride, hydrochloric acid, sodium hydroxide).

Myaesthenia gravis
Severe respiratory insufficiency
Sleep apnoea syndrome
Severe hepatic impairment

Side Effects

The most common adverse effects are severe drowsiness, respiratory depression and nausea and vomiting.
Others have been reported to occur (very rarely) following parenteral doses of midazolam so may be of relevance to oromucosal administration: agitation, aggression, anger, confusional state, euphoric mood, hallucination, hostility, movement disorder, physical assault, anterograde amnesia, ataxia, dizziness, headache, seizure, paradoxical reactions, bradycardia, cardiac arrest, hypotension, vasodilatation, apnoea, dyspnoea, laryngospasm, respiratory arrest, constipation, dry mouth, fatigue and hiccups.

Treatment of overdose

Midazolam overdose poses an increased risk if the patient has a pre-existing respiratory or cardiac insufficiency, or when combined with other CNS depressants (including alcohol).

Overdoses of buccal midazolam may be manifested by one or more of the following;

excessive sleepiness, confusion, low blood pressure, shallow breathing, excitation.

Inducing vomiting/ gastric lavage are generally not recommended as routine management in overdose[5]. Activated charcoal may be given within one hour of oral administration to reduce absorption from stomach if considered appropriate. Flumazenil, which is a short-acting benzodiazepine antagonist, may be considered as an antidote. **Contact the UK National Poisons Information Service for advice**.

The manufacturer's summary of product characteristics (SPC) and the most current edition of the British National Formulary for Children should be consulted for full information on contra-indications, warnings, side-effects and drug interactions.

References

1. Buccolam® (ViroPharma SPRL) Summary of Product Characteristics, September 2011
2. Shared care guidelines for prescribing buccal midazolam (Epistatus) in Adults – Bournemouth, Dorset and Poole Prescribing Forum June 2011
3. JEC guideline on training standards for the administration of buccal midazolam. Joint Epilepsy Council (2012)
4. The Epilepsies: the diagnosis and management of the epilepsies in adults and children in primary and secondary care, NICE CG 137, January 2012
5. Personal communication with Steve Jones at UK National Poisons Information Service – 28th June 2012
6. Personal communication with Rachel Hopkins, Consultant Pharmacist, PDC Healthcare, ViroPharma – 29th June 2012

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