PrescQIPP Community Interest Company

Buccal midazolam (SPOT-List)

Midazolam ranks as the eighth highest spend on the PrescQIPP SPOT-List (**S**pecials **P**rescribing **O**ptimisation **T**ool) despite a licensed buccal midazolam (Buccolam®) with a variety of strengths being available since October 2011. Buccolam® Oromucosal solution is licensed for the treatment of prolonged, acute, convulsive seizures in infants, toddlers, children and adolescents (from three months to less than 18 years old).[1]

Recommendations

- Always use the licensed product Buccolam® rather than unlicensed special buccal midazolam or midazolam drops.
- If a child has previously been on an unlicensed buccal midazolam, if it is clinically appropriate and with support from the specialist, consider a change to the licensed product, Buccolam®.
- Ensure that Buccolam® is only used by parents/carers if the patient has a diagnosis of epilepsy.[1] If this is not the case, consider referral back to specialist for advice.
- For infants between 3-6 months of age treatment should be in a hospital setting where monitoring is possible and resuscitation equipment is available.[1] If the patient is this age or younger and has been prescribed midazolam, refer patient management and prescribing back to the specialist.
- Buccolam® can be a different strength to unlicensed preparations such as Epistatus. In some cases, this is due to the existence of different midazolam salts, e.g. maleate.[2,3]
- Ensure that if any switches are made from unlicensed products to Buccolam®, patients and carers have been counselled, and that this has been documented.
- Buccolam oromucosal solution is not licensed for use in adults over 18 years.

Safety

The National Reporting and Learning System (NRLS) published a signal in February 2012 - Prevention of harm with buccal midazolam. This signal addresses the risks involved with buccal midazolam preparations. Between the 1 April 2008 and 22 August 2011, 132 relevant medication incidents were reported; three were associated with severe harm, five with moderate harm and the remainder with no or low harm.[4]

Identified wrong dose errors include incidents where:

- 2.5ml (25mg) was prescribed when 0.25ml (2.5mg) was intended,
- 2.5mg to 5mg was prescribed however, 2.5ml of 10mg/ml strength (25mg) was administered; and,
- 0.5ml was prescribed, however, the pharmacy label stated ''give one 5ml spoonful''.

Other potential errors include:

- Where a product with a 'Luer' connector could be inadvertently administered via the IV route.
- A dosing error caused by transfer from unlicensed buccal midazolam 10mg/ml to licensed buccal midazolam 5mg/ml (Buccolam®).

A hospital paediatric unit has also recently published its experience of transferring patients to licensed Buccolam. One of the key points raised was the requirement to have only one product (specifically only one strength) of product available for use.[5] This would be to ensure no confusion during dosing, and should be considered prior to switching patients to licensed product.

Evidence base

NICE guidance - Epilepsies: diagnosis and management [CG137] published in January 2012, advocates the following;[6]

For prolonged or repeated seizures and convulsive status epilepticus:

- Only prescribe buccal midazolam or rectal diazepam for use in the community for children, young people and adults who have had a previous episode of prolonged or serial convulsive seizures.
- Administer buccal midazolam as first-line treatment in children, young people and adults with prolonged or repeated seizures in the community. Administer rectal diazepam if preferred or if buccal midazolam is not available. If intravenous access is already established and resuscitation facilities are available, administer intravenous lorazepam.

Important information from the manufacturer when switching to licensed Buccolam®:[7]

Buccolam® is supplied in age-specific, pre-filled, needle-free, oral syringes.

- Each syringe contains the correct dose prescribed for an individual patient and is contained within a protective plastic tube.
- Syringes are colour-coded according to the prescribed dose for a particular age range.
- The doctor should prescribe the appropriate dose for the individual patient

Table 1: Showing the products and doses available[1]

Label colour	Midazolam dose	Volume of pre-filed syringe	Age range	Number of syringes per pack
Yellow	2.5mg	0.5ml	3 months to < 1 year	4
Blue	5mg	1ml	1 year to < 5 years	4
Purple	7.5mg	1.5ml	5 years to < 10 years	4
Orange	10mg	2ml	10 years to < 18 years	4

Buccolam® is half the strength of some other unlicensed preparations. It contains the hydrochloride salt, whereas some other preparations contain the maleate salt of midazolam. Although there is some suggestion that the maleate salt may be better absorbed in the buccal cavity, there are adequate studies with midazolam hydrochloride to support the dosing schedule authorised for Buccolam®.[2]

Epistatus

Buccolam® contains midazolam hydrochloride 5mg in 1ml in pre-filled oral syringes of 2.5mg, 5mg, 7.5mg and 10mg.

Epistatus contains midazolam maleate 10mg in 1ml.[2] It is a preparation in 5ml multi-dose bottle and a range of pre-filled syringes.[8] This is an unlicensed product available as a 'special'.[8]

The licence application for Epistatus was withdrawn after the MHRA requested that Special Products develop a pre-filled syringe preparation of Epistatus. The MHRA considered there is a risk of overdose in an emergency situation with the multi-dose preparation, the subject of the original licence application.[3]

In November 2015, Special Products re-submited a licence application to the MHRA for a pre-filled syringe preparation of Epistatus.[3] The age range for the current marketing authorisation application is ten to less than 18 years old.[8]

Use in adults

Buccolam oromucosal solution is not licensed for use in adults over 18 years. Unlicensed midazolam oromucosal formulations are available and may have different doses. The BNF states that for treatment of febrile convulsions in adults, the dose of buccal midazolam is 10mg, then 10mg after ten minutes if required.[3] The NICE clinical guideline on diagnosis and management of epilepsies states that buccal midazolam should be used as first line treatment in children, young people and adults for treating prolonged or repeated seizures and convulsive status epilepticus in the community.[6] In view of the required dose and all buccal midazolam formulations being unlicensed in adults, 10mg Buccolam would be appropriate in adults. In cases where a dose above 10mg is required, it may not be appropriate to use Buccolam and alternative unlicensed midazolam may be required, these cases should be looked at case by case, and wherever possible prescribed and supplied by the specialist.

Costs and savings

The highest spend on midazolam is for midazolam liquid special 50mg/5ml, accounting for nearly a third of the spend on prescribing liquid midazolam. This strength is likely to be for Epistatus (midazolam special order product). The current price directly from the manufacturer for 50mg/5ml is £45 for four syringes.[8] They have advised that the pricing for community pharmacies is a bit more complicated because the product is distributed via a third party and therefore the transfer pricing may not reflect the end price to the market.[8] A random price check with a community pharmacist, was £264, however this may be more or less depending on the pricing scheme via the wholesaler.

The annual spend in England and Wales for midazolam buccal liquid products is over £5.3 million of which over £3.4 million is for specials (ePACT March to May 2016). If reviewing appropriateness of prescribing and continued need of unlicensed preparations resulted in a 50% reduction in prescribing, **this could release over £1.7 million savings across England and Wales. This equates to approximately £2,856 per 100,000 patients.**

References

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Additional PrescQIPP resources

Data pack

Available here: https://www.prescqipp.info/resources/category/325-buccal-midazolam-spot-list

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Non-subscriber publication January 2017.

Contact help@prescqipp.info with any queries or comments related to the content of this document.