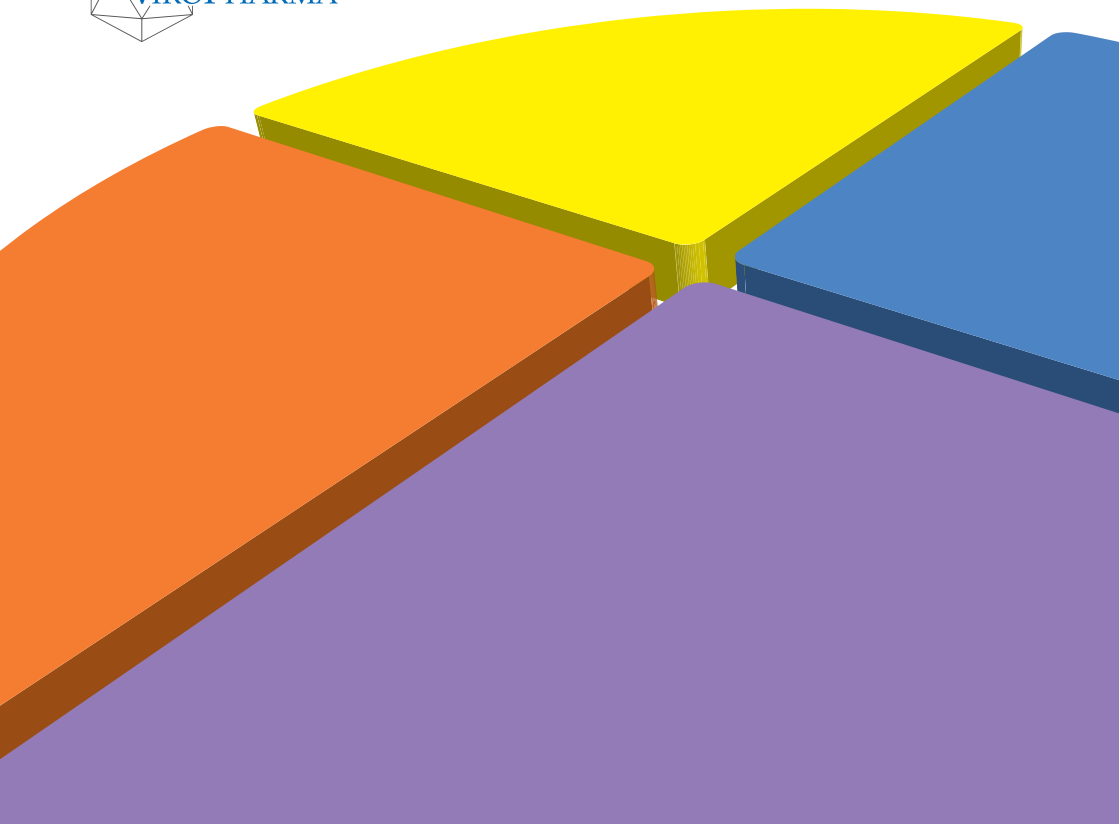
BUCCOLAM®▼
(midazolam oromucosal solution)

BUCCOLAM is the first and only licensed oromucosal midazolam indicated for the treatment of prolonged, acute, convulsive seizures in infants, toddlers, children and adolescents (from 3 months to <18 years of age).

BUCCOLAM must only be used by parents/carers where the patient has been diagnosed to have epilepsy.

For infants 3–6 months of age treatment should be in a hospital setting where monitoring is possible and resuscitation equipment is available.

VIROPHARMA™



Pre-filled syringes of BUCCOLAM® (midazolam oromucosal solution)

- BUCCOLAM is supplied in pre-filled, ready-to-use, plastic, oral syringes and should be administered into the space between the gum and the cheek (oromucosal administration).
- Each pack of BUCCOLAM contains four single-use syringes, each containing the same dose of medication, individually packed in protective plastic tubes. A leaflet is also included to provide further information about the product.
- The recommended dose of BUCCOLAM depends on the age of the patient. Therefore, BUCCOLAM is supplied in four different unit-dose, age-specific, colour-coded, pre-filled oral syringes (please see below).

Colour-coding of the different doses of BUCCOLAM

Label colour	Age range	Midazolam dose
Yellow	3 months to <1 year[a]	2.5 mg
Blue	1 to <5 years	5 mg
Purple	5 to <10 years	7.5 mg
Orange	10 to <18 years	10 mg

[a]For infants 3–6 months of age treatment should be in a hospital setting where monitoring is possible and resuscitation equipment is available

IMPORTANT:

BUCCOLAM does not require special storage but should be kept out of the sight and reach of children. Do not refrigerate or freeze.

The dosing instructions provided by a healthcare professional should be followed at all times.

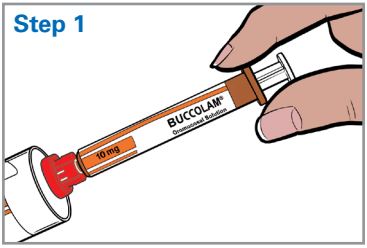
Please consult the Patient Information Leaflet found within the BUCCOLAM product box for further information, including contraindications, interactions, precautions and warnings, side effects, overdose and pregnancy.

How to administer BUCCOLAM® (midazolam oromucosal solution)

Before administering BUCCOLAM it is important to:

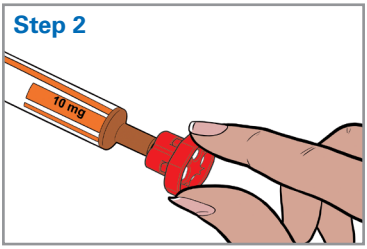
- Check the expiry date
- Check that the dose is correct for the patient, i.e. Is the syringe the correct dose and corresponding colour as prescribed for the patient's age?

Step 1



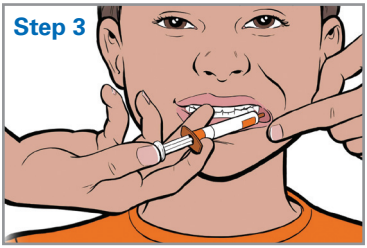
Break the tamper-proof seal and remove the syringe from the protective plastic tube.

Step 2



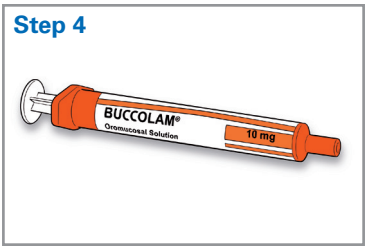
Remove and discard the oral syringe cap before use to avoid choking. Do not put a needle on the oral syringe. BUCCOLAM must not be injected. Each oral syringe is pre-filled with the exact dose you need to give for *one* treatment.

Step 3



Carefully insert the syringe into the space between the gum and the cheek. Administer the full amount of BUCCOLAM by slowly pressing the plunger of the syringe. If necessary, for larger volumes of BUCCOLAM and/or smaller patients, approximately half the dose should be given slowly into one side of the mouth, then the remainder given slowly into the other side.

Step 4



Keep the empty syringe, as you may need to give it to a healthcare professional to provide information on the dose received by the patient. If the seizure has not stopped within 10 minutes, call for emergency medical assistance.

General advice for administration of BUCCOLAM® (midazolam oromucosal solution)

- Loosen any clothing, ties or scarves that are tight around the neck to make the child more comfortable.
- Allow the child's body to move and do not try to stop the seizure with restraints, as it will be impossible. Only move the child if there is some form of danger in the immediate vicinity, such as deep water or an open flame. Remove all sharp objects from the area to prevent injury.
- After administering BUCCOLAM, do not touch the child's mouth or put anything in it, including water or medicine used to treat seizures, as it may cause the child to choke.
- Place a soft object underneath the child's head, if possible. A pillow, coat or sweatshirt may be a good option to help prevent further trauma to the head.
- Keep track of the amount of time the seizure lasts and watch for any specific symptoms, such as changed breathing patterns. The healthcare professional is likely to want to know the details of the seizure to best treat the patient.
- Ask other people who are around to stay calm and give the child plenty of room. Explain that the child is having a seizure, which is out of his/her control.
- Be calm and stay by the child's side until the seizure is over and the child has regained consciousness. They may be confused and tired or may feel embarrassed. Reassure them and be patient while they rest and regain strength.
- If the seizure does not stop do not give another dose of BUCCOLAM, but call for an ambulance.
- Do not give the child another dose of BUCCOLAM if they vomit.
- Do not give BUCCOLAM to children younger than 3 months of age.

BUCCOLAM®▼ (midazolam oromucosal solution) Abbreviated Prescribing Information (UK version)

Please refer to the Summary of Product Characteristics for full product information.

BUCCOLAM® oromucosal solution

Presentations: Pre-filled oral syringes containing 2.5 mg, 5 mg, 7.5 mg and 10 mg midazolam.

Indication: Treatment of prolonged, acute, convulsive seizures in infants, toddlers, children and adolescents (from 3 months to <18 years).

Dose and Administration:

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

*Where monitoring is possible and resuscitation equipment is available.

Treatment: BUCCOLAM must only be used by parents/carers where the patient has been diagnosed to have epilepsy.

Parents/carers should only administer a single dose of midazolam.

Children under 3 months: Not recommended.

Patients with renal impairment: No dose adjustment is required (see SmPC).

Patients with hepatic impairment: BUCCOLAM is contraindicated in patients with severe hepatic impairment.

Contraindications: Hypersensitivity to the active substance, to benzodiazepines or to any of the excipients, myasthenia gravis, severe respiratory insufficiency, sleep apnoea syndrome, severe hepatic impairment.

Pregnancy: The potential risk during pregnancy is unknown, however, 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.

Lactation: Midazolam passes in low quantities (0.6%) into breast milk and therefore it may not be necessary to stop breastfeeding following a single dose of midazolam.

Warnings and precautions: Midazolam should be used with caution in patients with chronic respiratory insufficiency because midazolam may further depress respiration.

Given the higher metabolite to parent drug ratio in younger children, a delayed respiratory depression as a result of high active metabolite concentrations in the 3–6 months age group cannot be excluded.

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 clearance of midazolam may be decreased.

Debilitated patients are more prone to the central nervous system 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.

Drug Interactions: Midazolam is metabolised by 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. Pharmacokinetic interactions with CYP3A4 inhibitors or inducers are more pronounced for oral as compared to oromucosal or parenteral midazolam as CYP3A4 enzymes are also present in the upper gastro-intestinal tract. After oromucosal administration, only systemic clearance will be affected. After a single dose of oromucosal midazolam, the consequence on the maximal clinical effect due to CYP3A4 inhibition will be minor while the duration of effect may be prolonged. Hence, careful monitoring of the clinical effects and vital signs is recommended during the use of midazolam with a CYP3A4 inhibitor even after a single dose.

Adverse reactions: Reported with midazolam are: Common (≥1/100 to <1/10): sedation, somnolence, depressed levels of consciousness, respiratory depression, nausea and vomiting. Uncommon (≥1/1,000 to <1/100): pruritus, rash and urticaria. Very rare (≤1/10,000) adverse reactions are listed in the SmPC.

Legal Category: POM.

Basic NHS Price:

2.5 mg	£82.00
5 mg	£85.50
7.5 mg	£89.00
10 mg	£91.50

MA Number:

2.5 mg:	EU/1/11/709/001
5 mg:	EU/1/11/709/002
7.5 mg:	EU/1/11/709/003
10 mg:	EU/1/11/709/004

Further Information from Marketing Authorisation Holder: ViroPharma SPRL, Rue Montoyer 47, 1000 Brussels, Belgium

Date of Preparation: September 2011

Adverse events should be reported. Reporting forms and information can be found at www.yellowcard.gov.uk. Adverse events should also be reported to ViroPharma Ltd on: 0207 572 1222

Visit our website for more information: **www.viropharma.com**

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