BUCCOLAM® (midazolam) 2.5 mg, 5 mg, 7.5 mg & 10 mg oromucosal solution PRESCRIBING INFORMATION.
Refer to Summary of Product Characteristics (SmPC) before prescribing.

Presentation: Pre-filled oral syringes containing midazolam (as hydrochloride) 2.5 mg in 0.5 ml solution, 5 mg in 1 ml solution, 7.5 mg in 1.5 ml solution and 10 mg in 2 ml solution for oromucosal use. **Indication:** Treatment of prolonged, acute, convulsive seizures in infants, toddlers, children and adolescents (from 3 months to <18 years). BUCCOLAM must only be used by parents/carers where the patient has been diagnosed to have epilepsy. For infants between 3-6 months of age treatment should be in a hospital setting where monitoring is possible and resuscitation equipment is available. **Dosage and administration:** BUCCOLAM is for oromucosal use.The full amount of solution should be inserted slowly into the space between the gum and the cheek. If necessary, for larger volumes and/or smaller patients, approximately half the dose should be given slowly into one side of the mouth, then the other half given slowly into the other side.

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 received by the patient.A second or repeat dose when seizures re-occur after an initial response should not be given without prior medical advice. The oral syringe cap should be removed before use to avoid risk of choking. *Children under 3 months:* The safety and efficacy in children aged 0-3 months has not been established. *Patients with renal impairment:* No dose adjustment is required (see SmPC), however, BUCCOLAM should be used with caution in patients with chronic renal failure as elimination of midazolam may be delayed and the effects prolonged. *Patients with hepatic impairment:* Hepatic impairment reduces the clearance of midazolam with a subsequent increase in terminal half-life. Careful monitoring is recommended (see SmPC). BUCCOLAM is contraindicated in patients with severe hepatic impairment. **Contraindications:** Hypersensitivity to the active substance, benzodiazepine or to any of the excipients. Patients suffering from myasthenia gravis, severe respiratory insufficiency, sleep apnoea syndrome and severe hepatic impairment. **Warnings and precautions:** Midazolam should be used with caution in patients with chronic respiratory insufficiency because midazolam may further depress respiration. Delayed respiratory depression as a result of high active metabolite concentrations in the 3–6 months age group cannot be excluded. The use of BUCCOLAM in this age group should be limited for use only under the supervision of a health care professional where resuscitation equipment is available. 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. **Interactions:** Midazolam is metabolised by CYP3A4. Medicinal products that inhibit or induce CYP3A4 have the potential to respectively increase and decrease the plasma concentrations of midazolam 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 gastrointestinal tract. *Anaesthetics and narcotic analgesics:* Fentanyl may reduce midazolam clearance; *Antiepileptics:* Co-administration may cause enhanced sedation or respiratory or cardiovascular depression. Midazolam may interact with other hepatically metabolised medicinal products, e.g. phenytoin, causing potentiation; *Calcium-channel blockers:* May either reduce clearance of midazolam and potentiate its action; *Dopaminergic agents*: Midazolam may cause inhibition of levodopa; *Muscle relaxants:* Midazolam may cause potentiation of muscle relaxants, with increased CNS depressant effects; *Nabilone:* Co-administration with midazolam may cause enhanced sedation or respiratory and cardiovascular depression; *Ulcer-healing medicinal products*: Cimetidine, ranitidine and omeprazole have been shown to reduce clearance of midazolam and may potentiate its action; *Xanthines:* Metabolism of midazolam is accelerated by xanthines. *Grapefruit juice:* Reduces the clearance of midazolam and potentiates its action. Please read the SmPC for further information on drug interactions

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

Fertility, pregnancy and lactation: Midazolam may be used during pregnancy if clearly necessary. The

risk for newborn infants should be taken into account in the event of administration of midazolam in the third trimester of pregnancy. *Breast Feeding*: 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. **Effects on ability to drive and use machines**: Midazolam has a major influence on the ability to drive and use machines. After receiving midazolam, the patient should be warned not to drive a vehicle or operate a machine until completely recovered. **Undesirable effects:** *Common* (≥1/100 to <1/10): sedation, somnolence, depressed levels of consciousness, respiratory depression, nausea and vomiting. Other serious undesirable effects:angioedema. **Refer to the SmPC for details on full side effect profile and interactions. UK Basic NHS price:** Per pack of 4 oral syringes: 2.5 mg -£82.00, 5 mg- £85.50, 7.5 mg- £89.00, 10 mg- £91.50.

Legal Classification: POM. **Marketing authorisation (MA):** PLGB 16869/0017-0020. **Name and address of MA holder:** Laboratorios Lesvi S.L. Avda Barcelona, 69, 08970 Sant Joan Despí, Barcelona, Spain.

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UK: Adverse events should be reported to the Medicines and Healthcare products Regulatory Agency. Reporting forms and information can be found at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.
Ireland: Adverse events should be reported to the Pharmacovigilance Unit at the Health Products Regulatory Authority (medsafety@hpra.ie). Information about Adverse Event reporting can be found on the HPRA website (www.hpra.ie).
UK & Ireland: Adverse events should also be reported and additional information on our products is available on request from Neuraxpharm UK Ltd pv-uk@neuraxpharm.com