SyriMed

MIPROSED

(Midazolam)

5mg/ml Oral Solution

Alcohol and Preservative Free

A simple choice for child sedation in minor procedures

Orange Flavoured

INTRODUCING

THERAPEUTIC INDICATIONS

Miprosed is indicated in children aged 6 months to 14 years for:

- Sedation and anxiolysis prior to diagnostic, surgical, therapeutic or endoscopic procedures.
- Premedication before induction of general anaesthesia

DOSING INFORMATION

- Children (6 months to 14 years): 0.25mg/kg to 0.5mg/kg administered 15-30 minutes before the intervention or the induction of anaesthesia. The dose should be adapted to the patient's weight and administered rounded to the nearest syringe graduation in millilitres. Maximum dose should not exceed 20mg.
- Obese children: Use actual body weight up to the maximum limit of 20mg.
- General fasting guidelines should be respected before sedation with Miprosed.

Advantages of Miprosed

Orange flavouring

- Easy oral administration via oral dosing syringe.

Licensed product

Single use bottle

Preservative free
Alcohol free

- Can be administered alone or given as a drink.
- Able to be mixed with apple juice or diluted blackcurrant cordial.

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When compared against IV Midazolam in endoscopy

Khodadad et al. compared oral Midazolam (0.5 mg/kg, max dose 10mg) with intravenous (IV) Midazolam (0.1 mg/kg, max dose 2.5mg) in 119 children undergoing upper GI endoscopy, in a randomised double blinded study [1]

The level of sedation was not significantly different between the two groups

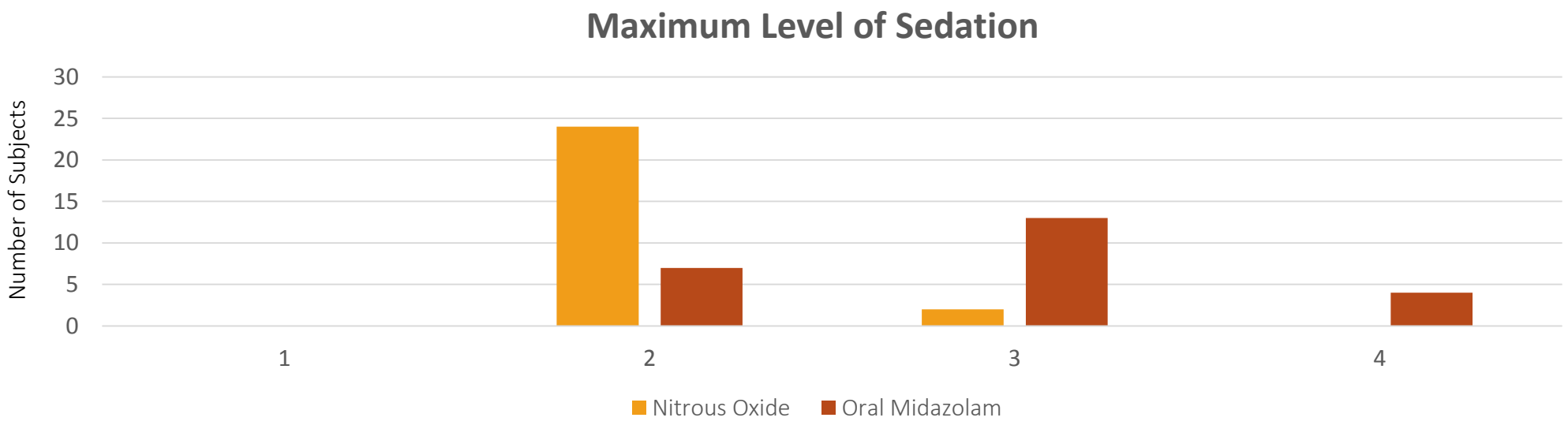
Time to return to full consciousness was similar **24.4±7.3 minutes in oral midazolam and 24.4±7.9 minutes in IV midazolam**)

COMPARISON

1. Khodadad et al., Acta Med Iran. 2016 Sep;54(9):576-582

Midazolam oral solution compared against nitrous oxide in orthodontic extractions of permanent teeth

In a randomised, controlled, crossover trial, 26 children (mean age 12.5 years) were administered nitrous oxide and oxygen (30% / 70%) or oral midazolam (0.5 mg/kg). Authors concluded that the mean level of sedation was higher in the oral midazolam group.[1]



The Maximum levels of sedation using the Brietkopf and Buttner classification of emotional status. Results are represented as the number of subjects scoring a maximum score of; 1 (awake, restless), 2 (awake, calm), 3(Tired, hardly moving), 4 (drowsy, without reaction hardly moving).

1. Wilson KE, et al.,. Br Dent J. 2002 Apr 27;192(8):457-62

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COMPARISON

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For relief of anxiety in minor surgical procedures

In clinical study in children aged 1 to 10 years undergoing 0.5 -6cm laceration repairs who received oral midazolam 0.5mg/kg Authors reported a single dose of midazolam resulted in reduced anxiety.[1]

1. Connors K et al., Annals of Emergency Medicine, 1994: 24; 1074-79

STUDIES

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Safety of oral Midazolam for sedation

In a prospective case study involving 510 children ASA class I to III aged 13months to 11 years undergoing dental procedures and given 0.5mg/kg oral midazolam reported that:

- All children maintained arterial oxygen saturation >95% throughout treatment
- Pulse rate throughout procedure within normal range for all children [1]

1. Lourenco – Matharu L & Roberts G British Dental Journal 2010; 209: E12

STUDIES

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As a premedication for general anaesthesia

At least 24 clinical studies have been conducted to compare oral midazolam to placebo or against other agents (e.g. clonidine, dexmedetomidine, intranasal midazolam, butorphanol, triclofos sodium, chloral hydrate) as premedication prior to general anaesthesia,.

Participants pre-sedated with oral midazolam were more frequently judged to be adequately sedated for IV placements compared to placebo (90% vs 41%, P<0.0001). [1]

93.33% children who received oral midazolam achieved adequate sedation when compared to 60% who had received triclofos sodium (P = 0.002). [2]

STUDIES

1. Liacouras et al., Gastrointest Endosc. 1998 Jun;47(6):455-60
2. Radhika et al., Indian J Anaesth. 2016;60(6):415-419. doi:10.4103/0019-5049.183389

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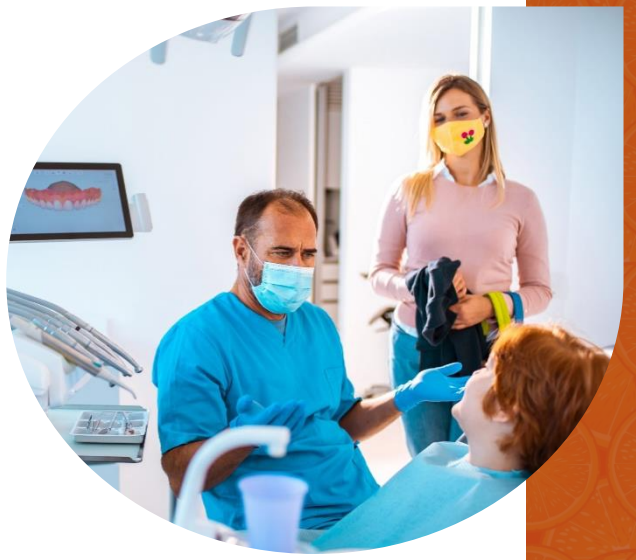
Guidance

The 2015 report of the Intercollegiate Advisory Committee for sedation in Dentistry of the UK Dental Faculties of the Royal Colleges of Surgeons and the Royal College of Anaesthetists entitled ‘Standards for conscious sedation in the provision of dental care’ created a national standard for the use of conscious sedation in care delivery.

In the report it is stated that midazolam is now considered the first choice agent for oral sedation. Historically temazepam was the first choice, but has been largely superseded by midazolam (IACSD 2015).



GUIDANCE

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Patient Profile

Miprosed aims to reduce anxiety produces sedation in children with:

- Efficacy as a sedative demonstrated in autistic children undergoing dental procedures[1]
- Children undergoing endoscopy procedures
- Dental/ oral surgery
- In children undergoing minor surgical procedures in A&E e.g laceration repair

[1]Pisalchaiyong T, Trairatvorakul C and Jirakijja J et al. Comparison of the effectiveness of oral diazepam and midazolam for the sedation of autistic patients during dentaltreatment. Pediatr Dent 2005; 27(3): 198-206.

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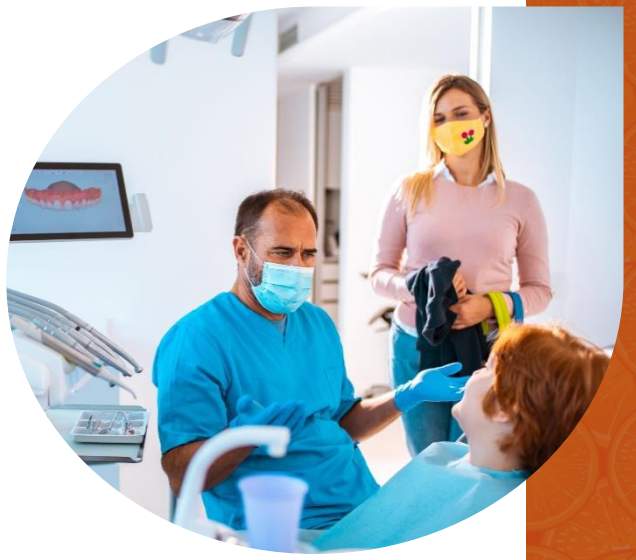
Summary

- Licensed oral solution
- First choice for oral sedation in dental surgery[1]
- Use of oral midazolam is well established with over 20 years use for oral sedation before diagnostic therapeutic, other surgical procedures and as premedication before general anesthesia
- Orange flavoured to mask bitter taste of midazolam
- Alcohol and Preservative free
- Easy to administer using oral dosing syringe
- Dose can be mixed with apple juice or diluted blackcurrant cordial and given as a drink
- Individual patient pack to minimise risk of administration error



GUIDANCE

[1]IACSD (Intercollegiate Advisory Committee for Sedation in Dentistry). Standards for conscious sedation in the provision of dental care. 2015.

Prescribing Information

Please refer to full SmPC before prescribing.

Product Name: Miprosed 5mg/ml Oral Solution
Composition: Each ml of oral solution contains 5mg midazolam. For the full list of excipients see SmPC.

Indications: Children aged 6 months to 14 years: Sedation and anxiolysis prior to diagnostic, surgical, therapeutic or endoscopic procedures. Premedication before induction of general anaesthesia.

Posology and method of administration: Oral use. Children (6 months to 14 years):0.25mg/kg to 0.5mg/kg administered 15-30 minutes before the intervention or the induction of anaesthesia. The dose should be adapted to the patient's weight and administered rounded to the nearest syringe graduation in millilitres. Maximum dose should not exceed 20mg. Obese children: Use actual body weight up to the maximum limit of 20mg. Miprosed may be mixed with and administered in apple juice and diluted blackcurrant cordial. General fasting guidelines should be respected before sedation with Miprosed

Contraindications: Hypersensitivity to midazolam or to any of the excipients; Severe hepatic impairment; Severe respiratory failure or acute respiratory depression; Myasthenia gravis; Sleep apnoea; Anatomical respiratory impairment or lung diseases.
Warnings and precautions for use: Administration only by experienced physicians in a setting fully equipped for the monitoring and support of respiratory and cardiovascular function and by persons specifically trained in the recognition and management of expected adverse events. Caution in patients with hepatic impairment, heart failure or chronic renal failure. Caution in patients in poor general health. Concomitant use of midazolam and opioids or benzodiazepines may result in sedation, respiratory depression, coma and death. Concomitant prescribing should be reserved for patients for whom alternative treatment options are not possible; if prescribed, patients should be followed closely for signs and symptoms of respiratory depression and sedation and be informed of these symptoms. Caution in patients with chronic respiratory insufficiency. Miprosed should not be used in children aged under 6 months. Debilitated patients are more prone to the central nervous system effects of benzodiazepines and lower doses may be required. Avoid in patients with a medical history of alcohol or drug abuse. Combined use of midazolam and alcohol and/or central nervous system depressants should be avoided. Midazolam may cause anterograde amnesia. Paradoxical reactions such as agitation, involuntary movements (including tonic/clonic movements and muscle tremor), hyperactivity, hostility, rage reaction, aggression, paroxysmal excitement have been reported. Should such reactions occur, the response to midazolam and all other drugs including local anaesthetics should be evaluated before proceeding. It is recommended that children receiving oral midazolam are discharged post-surgery accompanied by a parent or guardian.

Interactions with other medicinal products: Inhibitors and inducers of CYP3A4. Pharmacokinetic interactions with CYP3A4 inhibitors or inducers are more pronounced for oral as compared to oromucosal or parenteral midazolam. 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. The effect of CYP3A4 inhibitors may be larger in infants. Rifamipicin, St John's Wort, Fentanyl, Carbamazepine, Phenytoin, Diltiazem, Verapamil, Cimetidine, Ranitidine, Omeprazole, Xanthines, Aprepitant, Levodopa, Muscle relaxants, Nabilone, Grapefruit juice, Caffeine and incompatible with cranberry juice. Azole antifungals (ketoconazole, voriconazole, fluconazole, posaconazole, itraconazole), Erythromycin, Clarithromycin, Propiverine, Fluvoxamine, Nefazodone, Glucocorticoids, Protease inhibitors, Efavirenz, Atorvastatin. Sedative/hypnotic medicinal products and CNS depressants, including opiate derivatives (used as analgesics, antitussives or substitutive treatments), antipsychotics, other benzodiazepines used as anxiolytics or hypnotics, barbiturates, propofol, ketamine, etomidate; sedative antidepressants, non-recent H1-antihistamines and centrally acting antihypertensive medicinal products. Alcohol (including alcohol-containing medicinal products); intake should be strongly avoided with midazolam. Midazolam decreases the minimum alveolar concentration (MAC) of inhalation anaesthetics.

Fertility, pregnancy and lactation: Midazolam may be used during pregnancy if clearly necessary.
No available data on the use of midazolam in women during the first two trimesters of pregnancy. At therapeutic doses, the active substance passes into the breast milk in low quantities. It may not be necessary to stop breast feeding following a single dose of midazolam.

Driving ability or use of machines: Sedation, amnesia, impaired attention and impaired muscular function may adversely affect the ability to drive, ride a bicycle or 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: Agitation, Somnolence, Paradoxical reactions. It has not been possible to estimate the frequency of adverse events from the available clinical studies reporting the use of oral midazolam as a premedicant before induction of anaesthesia. The adverse events that have been reported in these clinical studies in patients receiving oral midazolam include: nausea, vomiting, salivation, hypoxia, hypertension, tachycardia, agitation, vertigo, euphoria, excitation, restlessness and nocturnal enuresis. See SmPC for full list of side-effects.

Legal Category: POM.
NHS Price: £18.00 for 7.5ml bottle
Marketing Authorisation Number: PL 39307/0096
Marketing Authorisation Holder: Syri Limited t/a Syrimed, Unit 4, Bradfield Road, Ruislip, HA4 0NU.
Date of prescribing information: 20/04/2021

Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard. Adverse events should also be reported to the Medical Information Department at SyriMed by Telephone: 0208 515 3700 or Email: medinfo@thamelabs.co.uk.

Item code: 2021/08

Date of Preparation: 25/05/2021

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PRESCRIBING INFORMATION