Medicines & Healthcare products
Regulatory Agency

Public Assessment Report

National Procedure

Midazolam 2.5 mg oromucosal solution
Midazolam 5 mg oromucosal solution
Midazolam 7.5 mg oromucosal solution
Midazolam 10 mg oromucosal solution

midazolam (as midazolam hydrochloride)

PLGB 16869/0025-0028

Neuraxpharm Pharmaceuticals, S.L.

LAY SUMMARY

Midazolam 2.5 mg oromucosal solution
Midazolam 5 mg oromucosal solution
Midazolam 7.5 mg oromucosal solution
Midazolam 10 mg oromucosal solution
midazolam (as midazolam hydrochloride)

This is a summary of the Public Assessment Report (PAR) for Midazolam 2.5 mg, 5 mg, 7.5 mg and 10 mg oromucosal solution. It explains how these products were assessed and their authorisation recommended, as well as their conditions of use. It is not intended to provide practical advice on how to use these products.

These products will be referred to as Midazolam oromucosal solution in this lay summary for ease of reading.

For practical information about using Midazolam oromucosal solution, patients should read the Patient Information Leaflet (PIL) or contact their doctor or pharmacist.

What is Midazolam oromucosal solution and what is it used for?
These applications are the same as Buccolam 2.5 mg, 5 mg, 7.5 mg and 10 mg oromucosal solution (PLGB 16869/0017-0020) which are already authorised.

The Company responsible for Buccolam 2.5 mg, 5 mg, 7.5 mg and 10 mg Oromucosal Solution has agreed that its scientific data can be used as the basis for the grant of identical licences for Midazolam oromucosal solution.

Midazolam oromucosal solution is used to stop a sudden, prolonged, convulsive, seizure in infants, toddlers, children and adolescents (from 3 months to less than 18 years of age).

In infants from 3 months to less than 6 months it should only be used in a hospital setting where monitoring is possible and resuscitation equipment is available.

These medicines must only be used by parents/carers where the child has been diagnosed to have epilepsy.

How does Midazolam oromucosal solution work?
These medicines contain the active substance midazolam (as midazolam hydrochloride). Midazolam belongs to a group of medicines known as benzodiazepines.

How is Midazolam oromucosal solution used?
The pharmaceutical form of these medicines is an oromucosal solution and the route of administration is oral solution.

The patient’s doctor will prescribe the appropriate dose of Midazolam oromucosal solution the child needs, generally according to the child’s age. The different doses each have a different colour, which is shown on the carton, the tube and the syringe containing the medicine.

Depending on age, the child will have received one of the following doses, in specifically colour labelled packaging:

The dose is the full contents of one oral syringe. The caregiver should not give more than one dose.

Toddlers aged from 3 months to less than 6 months should only be treated in a hospital setting where monitoring is possible and resuscitation equipment is available.

Preparing to give this medicine
If the child is having a seizure, the parent/carer should allow the child's body to move freely; the parent/caregiver should not try to restrain them. The parent/carer should only move the child if they are in danger from, for example, deep water, fire or sharp objects. The carer should support the child's head with something soft, such as a cushion or their (the carer's) lap. The parent/carer should check that the medicines is the correct dose for the child, according to their age.

How to give this medicine
The parent/carer should ask a doctor, pharmacist or nurse to show them how to take or administer this medicine. The parent/carer should always check with the healthcare professor if they are not sure. The information on how to give this medicine is also shown on the tube label.

Midazolam oromucosal solution must not be injected. The carer should not attach a needle to the syringe

For further information on how Midazolam oromucosal solution are used, refer to the PIL and Summaries of Product Characteristics (SmPCs) available on the Medicines and Healthcare products Regulatory Agency (MHRA) website.

These medicines can only be obtained with a prescription.

The patient should always receive the medicine(s) exactly as their doctor/pharmacist has told them. The caregiver should check with their doctor or pharmacist if they are not sure.

What benefits of Midazolam oromucosal solution have been shown in studies?
The Midazolam oromucosal solution products are considered identical to the previously authorised products with the same benefits and risks. No new studies have been provided for Midazolam oromucosal solution; however, reference is made to the studies for Buccolam 2.5 mg, 5 mg, 7.5 mg and 10 mg Oromucosal Solution.

What are the possible side effects of Midazolam oromucosal solution?
For the full list of all side effects reported with these medicines, see Section 4 of the PIL or the SmPCs available on the MHRA website.

If a patient gets any side effects, they should talk to their doctor, pharmacist or nurse. This includes any possible side effects not listed in the product information or the PIL that comes with the medicines. Patients can also report suspected side effects themselves, or a report can be made on their behalf by someone else who cares for them, directly via the Yellow Card scheme at https://yellowcard.mhra.gov.uk or search for 'MHRA Yellow Card' online. By

reporting side effects, patients can help provide more information on the safety of these medicines.

The Midazolam oromucosal solution products are considered to be identical to the previously authorised products with the same benefits and risks.

Why were Midazolam oromucosal solution approved?
The MHRA decided that the benefits of Midazolam oromucosal solution are greater than the risks and recommended that these medicines are approved for use.

What measures are being taken to ensure the safe and effective use of Midazolam oromucosal solution?
As for all newly authorised medicines, a Risk Management Plan (RMP) has been developed for Midazolam oromucosal solution. The RMP details the important risks of Midazolam oromucosal solution, how these risks can be minimised, any uncertainties about Midazolam oromucosal solution (missing information), and how more information will be obtained about the important risks and uncertainties.

The following safety concerns have been recognised for Midazolam oromucosal solution:

Table 1: Summary of safety concerns

Summary of safety concerns	
Important identified risks	None.
Important potential risks	Aspiration/aspiration pneumonia. Choking/asphyxiation on syringe cap. Medication errors.
Missing information	Use in children < 6 months of age

The information included in the SmPCs and the PIL is compiled based on the available quality, non-clinical and clinical data, and includes appropriate precautions to be followed by healthcare professionals and patients. Side effects of Midazolam oromucosal solution are continuously monitored and reviewed including all reports of suspected side-effects from patients, their carers, and healthcare professionals.

An RMP and a summary of the pharmacovigilance system have been provided with these applications and are satisfactory.

Other information about Midazolam oromucosal solution
Marketing authorisations were granted in Great Britain on 18 June 2025.

The full PAR for Midazolam oromucosal solution follows this summary.

This summary was last updated in August 2025.

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I. INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the Medicines and Healthcare products Regulatory Agency (MHRA) considered that the applications for Midazolam 2.5 mg, 5 mg, 7.5 mg and 10 mg oromucosal solution (PLGB 16869/0025-0028) could be approved.

The products are approved for the following indication:

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

  Midazolam 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. See section 4.2 of the Summaries of Product Characteristics (SmPCs).

The name of the active substance is midazolam (as midazolam hydrochloride), which is a derivative of the imidazobenzodiazepine group. The free base is a lipophilic substance with low solubility in water. The basic nitrogen in position 2 of the imidazobenzodiazepine ring system enables midazolam to form the hydrochloride salt with acids. These produce a stable solution suitable for oromucosal administration. Midazolam has an anticonvulsant effect. It also exerts a sedative and sleep-inducing effect of pronounced intensity, and an anxiolytic and a muscle-relaxant effect.

These are national abridged applications approved under Regulation 56 of The Human Medicines Regulation 2012, as amended (previously Article 10c of Directive 2001/83/EC, as amended) as informed consent applications. The applications cross-refer to the reference products Midazolam 2.5 mg, 5 mg, 7.5 mg and 10 mg oromucosal solution (PLGB 16869/0017-0020).

No new non-clinical or clinical data have been supplied and none are required for these informed consent applications.

Suitable justification has been provided for non-submission of an Environmental Risk Assessment (ERA). As the applications are for identical versions of already authorised products, no increase in environmental exposure is anticipated and no ERA is required.

The MHRA has been assured that acceptable standards of Good Manufacturing Practice (GMP) are in place for these products at all sites responsible for the manufacture, assembly and batch release of these products.

A Risk Management Plan (RMP) and a summary of the pharmacovigilance system have been provided with these applications and are satisfactory.

National marketing authorisations were granted in the UK on 18 June 2025.

II. EXPERT REPORT

The applicant cross-refers to the data for Midazolam 2.5 mg, 5 mg, 7.5 mg and 10 mg oromucosal solution (PLGB 16869/0017-0020; Neuraxpharm Pharmaceuticals S.L.), to which these applications are claimed to be identical. This is acceptable.

III. ASSESSOR'S COMMENTS ON THE PRODUCT INFORMATION

Summaries of Product Characteristics (SmPCs)

The SmPCs are in line with those for Midazolam 2.5 mg, 5 mg, 7.5 mg and 10 mg oromucosal solution (PLGB 16869/0017-0020; Neuraxpharm Pharmaceuticals S.L.), dated 01/2024, except for differences in the indications to omit adult use.

PATIENT INFORMATION LEAFLET (PIL)

A mock-up leaflet has been provided which has been aligned, except for differences in the indications to omit adult use, with that for Midazolam 2.5 mg, 5 mg, 7.5 mg and 10 mg oromucosal solution (PLGB 16869/0017-0020; Neuraxpharm Pharmaceuticals S.L.), dated 11/2023.

LABEL

Label mock-ups have been provided.

IV. QUALITY ASPECTS

IV.1 Drug Substance

Drug substance specifications

The source of the active substance is in line with the cross-reference products. The proposed drug substance specification is consistent with the details registered for the cross-reference products.

IV.2. Drug Product

Name

The products have been named in line with current requirements.

Strength, pharmaceutical form, route of administration, container and pack sizes

Midazolam 2.5 mg, 5 mg, 7.5 mg and 10 mg oromucosal solution are available in amber, pre-filled needle-free oral syringes (polypropylene), each with a plunger (polypropylene) and an end cap (high density polyethylene), packed in a protective, capped plastic tube.

Strength	Volume of solution	Syringe volume	Age range	Label colour
2.5 mg	0.5 ml	1 ml	3 months to < 1 year	Yellow
5 mg	1 ml	3 ml	1 year to < 5 years	Blue
7.5 mg	1.5 ml	3 ml	5 years to < 10 years	Purple
10 mg	2 ml	3 ml	10 years to < 18 years	Orange

The products are available in two pack sizes:
- cartons containing 2 pre-filled syringes
- cartons containing 4 pre-filled syringes

Not all pack sizes may be marketed.

The appearance of the products is identical to that of the cross-reference products.

The proposed shelf life of the product is 18 months with the special storage conditions/with the recommended storage conditions 'Keep the oral syringe in the protective plastic tube. Do not refrigerate or freeze.'

The proposed packaging, shelf life and storage conditions are consistent with the details registered for the reference products.

Legal status
Prescription only medicine (POM)

Manufacturers
The proposed manufacturing sites are consistent with the details registered for the cross-reference products and evidence of Good Manufacturing Practice (GMP) compliance has been provided.

Qualitative and quantitative compositions
The composition of the proposed products are consistent with the details registered for the cross-reference products.

Manufacturing process & control of critical steps
The proposed manufacturing processes and process controls are consistent with the details registered for the reference products and the maximum batch size is stated.

Finished product release/shelf-life specifications
The finished product specifications at release and shelf-life are in line with the details registered for the cross-reference products.

TSE Compliance
No excipients of animal or human origin are used in the final products.

These products do not contain or consist of genetically modified organisms (GMO).

NON-CLINICAL ASPECTS
As these applications are submitted under Regulation 56 of The Human Medicines Regulation 2012, as amended, (as informed consent applications) no new non-clinical data have been supplied and none are required.

V. CLINICAL ASPECTS
As these applications are submitted under Regulation 56 of The Human Medicines Regulation 2012, as amended, (as informed consent applications) no new clinical data have been supplied and none are required.

VI. RISK MANAGEMENT PLAN (RMP)
The applicant has submitted an RMP, in accordance with the requirements of Regulation 182 of The Human Medicines Regulation 2012, as amended. The applicant proposes only routine pharmacovigilance and routine risk minimisation measures for all safety concerns. This is acceptable.

VII. USER CONSULTATION
A full colour mock-up of the PIL was provided with the applications in accordance with legal requirements, including user consultation.

VIII. OVERALL CONCLUSION, BENEFIT/RISK AND RECOMMENDATION
The quality of the products is acceptable, and no new non-clinical or clinical safety concerns have been identified. The applicant's products are identical to the cross-reference products.

The benefit/risk balance is, therefore, considered to be the same as for the cross-reference products and positive.

The Summaries of Product Characteristics (SmPCs), PIL and labelling are satisfactory, in line with current guidelines and consistent with the cross-reference products.

In accordance with legal requirements, the current approved GB version of the SmPCs and PILs for these products are available on the MHRA website.

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Steps taken after the initial procedure with an influence on the Public Assessment Report (non-safety variations of clinical significance).

Please note that only non-safety variations of clinical significance are recorded below and in the annexes to this PAR. The assessment of safety variations, where significant changes are made, are recorded on the MHRA website or European Medicines Agency (EMA) website. Minor changes to the marketing are recorded in the current SmPCs and/or PIL available on the MHRA website.

Application type	**Scope**	**Product information affected**	**Date of grant**	**Outcome**	**Assessment report attached Y/N**