Medicines & Healthcare products
Regulatory Agency

Public Assessment Report

National Procedure

Lorazepam 0.5 mg Tablets
Lorazepam 1 mg Tablets
Lorazepam 2.5 mg Tablets

lorazepam

PL 34424/0108 - 0110

Key Pharmaceuticals Ltd.

LAY SUMMARY

Lorazepam 0.5 mg Tablets
Lorazepam 1 mg Tablets
Lorazepam 2.5 mg Tablets
lorazepam

This is a summary of the Public Assessment Report (PAR) for Lorazepam 0.5 mg, 1 mg, and 2.5 mg Tablets. 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 Lorazepam Tablets in this lay summary for ease of reading.

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

What are Lorazepam Tablets and what are they used for?
The application for Lorazepam 0.5 mg Tablets is for a hybrid medicine. This means that this medicine is similar to the reference medicine, Lorazepam 2.5 mg Tablets (PL 17225/0011), albeit with certain differences. In this case, Lorazepam 0.5 mg Tablets, is lower strength (of the active substance), than the reference product.

The applications for Lorazepam 1 mg, and 2.5 mg Tablets (PL 34424/0109 – 0110) are for generic medicines. This means that these medicines are the same as, and considered interchangeable with, the reference medicines already authorised in the United Kingdom (UK) called Lorazepam 2.5 mg and 1 mg Tablets (PL 17225/0010 - 0011).

Lorazepam Tablets are prescribed as short-term therapy for anxiety (2-4 weeks) or sleeping difficulties due to anxiety. They may also be used as a sedative before surgery or operative dental treatment.

Lorazepam tablets are *not* to be used for longer than 4 weeks, to treat mild or moderate anxiety in adults or for anxiety/insomnia in children.

How do Lorazepam Tablets work?
Lorazepam Tablets contains the active substance, lorazepam which is a member of a group of medicines called benzodiazepines. It can help to relieve anxiety.

How are Lorazepam Tablets used?
The pharmaceutical form of these medicines is a tablet, and the route of administration is oral (by mouth).

Lorazepam tablets should be swallowed with water.

Adults (and children over 13 years of age)

- **Anxiety**: 1 to 4 mg daily in divided doses. The patient's doctor will tell them how often to take their tablets.
- **Sleeping Problems**: 1 to 2 mg before going to sleep. The patient should make sure that they will be able to sleep for 7 to 8 hours before taking their tablets.
- **Before Surgery**: 2 to 3 mg the night before the operation and 2 to 4 mg 1 or 2 hours before the operation.

Children (between 5 and 13 years of age)

- **Before Surgery**: The dose is usually between 0.5 and 2.5 mg (depending on the child's weight) at least 1 hour before the child's operation.
- Lorazepam is *not* recommended for the treatment of anxiety or sleeping problems in children. *Nor* is it recommended for children below 5 years of age.

Elderly or patients with liver or kidney problems

- Older patients may be given lower doses. They may respond to half the usual adult dose or less.

Lorazepam is usually prescribed for short courses of treatment, lasting from a few days to 4 weeks including a dose reduction at the end. This reduces the risk of becoming dependent on Lorazepam tablets or suffering unpleasant effects when the patient stops taking them.

The beneficial effect of Lorazepam tablets may be less apparent after several weeks of use. If the patient is given lorazepam for more than 4 weeks, their doctor might want to take blood samples occasionally to check their blood and liver, since drugs like lorazepam have occasionally affected blood and liver function.

For further information on how Lorazepam Tablets are used, refer to the PILs 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 take these medicines exactly as their doctor/pharmacist has told them. The patient or caregiver should check with their doctor or pharmacist if they are not sure.

What benefits of Lorazepam Tablets have been shown in studies?

As Lorazepam Tablets are hybrid/generic medicines, studies in healthy volunteers have been limited to tests to determine that these are bioequivalent to the reference medicines. Two medicines are bioequivalent when they produce the same levels of the active substance in the body.

What are the possible side effects of Lorazepam Tablets?

For the full list of all side effects reported with these medicines, see Section 4 of the PILs 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 PILs 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.

Because Lorazepam Tablets are hybrid/generic medicines, and are bioequivalent to the reference medicines, their benefits and possible side effects are taken as being the same as the reference medicines.

Why were Lorazepam Tablets approved?
It was concluded that Lorazepam Tablets have been shown to be bioequivalent to the reference medicines. Therefore, the MHRA decided that, as for the reference medicines, the benefits are greater than the risks and authorised that these can be approved for use.

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

There are no safety concerns associated with use of Lorazepam Tablets.

The information included in the SmPCs and the PILs 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 Lorazepam Tablets 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 Lorazepam Tablets
Marketing Authorisations for Lorazepam Tablets were granted in the United Kingdom (UK) on 06 November 2025.

The full PAR for Lorazepam Tablets follows this summary.

This summary was last updated in December 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 Lorazepam 0.5 mg, 1 mg, and 2.5 mg Tablets (PL 34424/0108 - 0110) could be approved.

The products are approved for the following indications:
For short term (2 - 4 weeks only) use (Adults *only*)

- Symptomatic relief of anxiety that is severe, disabling or subjecting the individual to unacceptable distress occurring alone or in association with insomnia or short term psychometric, organic or psychotic illness

As premedication (Adults and Children 5 years and above)

Before operative dentistry and general surgery

Not for use

- Long term (i.e. longer than 4 weeks)
- For mild/moderate anxiety
- For insomnia or anxiety in children

Lorazepam 0.5 mg, 1 mg, and 2.5 mg Tablets contain the active substance, lorazepam which is a benzodiazepine derivative with anxiolytic, sedative and hypnotic properties.

The application for Lorazepam 0.5 mg Tablets was approved under Regulation 52B of The Human Medicines Regulation 2012, as amended (previously Article 10(3) of Directive 2001/83/EC, as amended), as a hybrid medicinal product of a suitable originator product, Lorazepam 2.5 mg Tablets.

The applications for Lorazepam 1 mg, and 2.5 mg Tablets were approved under Regulation 51B of The Human Medicines Regulations 2012, as amended (previously Article 10(1) of Directive 2001/83/EC, as amended), as generic medicines of suitable originator medicinal products, Lorazepam 1 mg, and 2.5 mg Tablets, that have been licensed within the UK for a suitable time, in line with the legal requirements.

No new non-clinical studies were conducted, which is acceptable given that the applications are for hybrid/generic medicinal products of suitable reference products.

With the exception of the bioequivalence study, no new clinical studies were conducted, which is acceptable given that the applications are for hybrid/generic medicinal products of suitable reference products. The bioequivalence study was conducted in line with current Good Clinical Practice (GCP).

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.

Advice was sought from the Commission of Human Medicines (CHM) on 26 June 2025 because major objections were raised with respect to the quality aspects of the dossier. In response to the CHM, the applicant provided additional data, to address the points that had been raised. Following consideration of the responses and further data that were submitted, the approval of the Marketing Authorisation was recommended.

National marketing authorisations for Lorazepam 0.5 mg, 1 mg, and 2.5 mg Tablets were granted in the United Kingdom (UK) on 06 November 2025.

II QUALITY ASPECTS

II.1 Introduction

The active substance is lorazepam.
Three different strengths of tablets are available.
Each 0.5 mg, 1 mg and 2.5 mg tablet contains 0.5 mg, 1 mg and 2.5 mg lorazepam, respectively.

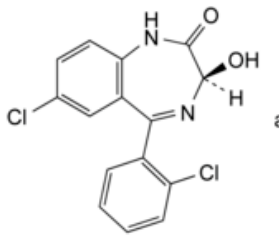
In addition to lorazepam, these products also contain the following excipients: microcrystalline cellulose, anhydrous lactose, polacrilin potassium and magnesium stearate.
1 mg strength also contains indigo carmine aluminium lake (E132).
2.5 mg strength also contains ferric oxide yellow (E172).

The finished products are packaged in Alu/Alu (OPA/Alu/PVC) blister packs and are available in pack-sizes of 28, 30, 56, 60 or 100 tablets.
Not all pack sizes may be marketed.

Satisfactory specifications and Certificates of Analysis have been provided for all packaging components. All primary packaging complies with the current regulations concerning materials in contact with food.

II.2 ACTIVE SUBSTANCE

rINN: lorazepam
Chemical Name: (3*RS*)-7-Chloro-5-(2-chlorophenyl)-3-hydroxy-1,3-dihydro-2*H*-1,4-benzodiazepin-2-one.
Molecular Formula: $C_{15}H_{10}Cl_2N_2O_2$
Chemical Structure:



and enantiomer

Molecular Weight: 321.2
Appearance: White or almost white, crystalline powder.
Solubility: Practically insoluble in water, sparingly soluble in ethanol (96 per cent), sparingly soluble or slightly soluble in methylene chloride.

Lorazepam is the subject of a European Pharmacopoeia monograph.

All aspects of the manufacture and control of the active substance are covered by a European Directorate for the Quality of Medicines and Healthcare (EDQM) Certificate of Suitability.

II.3 DRUG PRODUCTS

Pharmaceutical development
A satisfactory account of the pharmaceutical development has been provided.

Comparative *in vitro* dissolution profiles have been provided for the proposed and reference products.

All excipients comply with either their respective European/national monographs, or a suitable in-house specification. Satisfactory Certificates of Analysis have been provided for all excipients.

With the exception of anhydrous lactose, no excipients of animal or human origin are used in the final products. The supplier of lactose monohydrate has confirmed that it is sourced from healthy animals under the same conditions as milk for human consumption.

Confirmation has been given that the magnesium stearate used in the tablets is of vegetable origin.

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

Manufacture of the products
A description and flow-chart of the manufacturing method has been provided.

Satisfactory batch formulation data have been provided for the manufacture of the products, along with an appropriate account of the manufacturing process. The manufacturing process has been validated and has shown satisfactory results.

Finished Product Specifications
The finished product specifications at release and shelf-life are satisfactory. The test methods have been described and adequately validated. Batch data have been provided that comply with the release specifications. Certificates of Analysis have been provided for any working standards used.

Stability
Finished product stability studies have been conducted in accordance with current guidelines, using batches of the finished product stored in the packaging proposed for marketing. Based on the results, a shelf-life of 2 years, with the storage conditions ‘Store in the original package in order to protect from light’, is acceptable.

Suitable post approval stability commitments have been provided to continue stability testing on batches of finished product.

II.4 Discussion on chemical, pharmaceutical and biological aspects

The grant of marketing authorisations was recommended.

III NON-CLINICAL ASPECTS

III.1 Introduction
As the pharmacodynamic, pharmacokinetic and toxicological properties of lorazepam are well-known, no new non-clinical studies are required, and none have been provided. An overview based on the literature review is, thus, appropriate.

III.2 Pharmacology
No new pharmacology data were provided, and none were required for these applications.

III.3 Pharmacokinetics
No new pharmacokinetic data were provided, and none were required for these applications.

III.4 Toxicology
No new toxicology data were provided, and none were required for these applications.

III.5 Ecotoxicity/Environmental Risk Assessment
Suitable justification has been provided for non-submission of an Environmental Risk Assessment. As these are hybrid/generic applications of already authorised products, it is not expected that environmental exposure will increase following approval of the Marketing Authorisations for the proposed products.

III.6 Discussion on the non-clinical aspects
The grant of marketing authorisations was recommended.

IV CLINICAL ASPECTS

IV.1 Introduction
The clinical pharmacology, efficacy and safety of lorazepam are well-known. With the exception of data from the bioequivalence study, no new clinical data are provided or are required for these applications. An overview based on a literature review and a review of this study is, thus, satisfactory.

IV.2 Pharmacokinetics
In support of the applications, the applicant submitted the following bioequivalence study:

Bioequivalence Study
This study was an open label, balanced, randomised, two-treatment, two-period, two-sequence, single oral dose, crossover, bioequivalence study of Lorazepam 2.5 mg Tablets (test product) versus Lorazepam 2.5 mg Tablets (reference product) in normal, healthy, adult, human subjects under fasting condition.

After an overnight fast of at least 10 hours, subjects were administered single oral dose of either test or reference product. Blood samples were taken pre-dose and up to 72 hours post dose, with a washout period of 07 days between the treatment periods.

A summary of the pharmacokinetic results is presented below:

Table 1. Descriptive Statistics of Formulation Means for Lorazepam (N = 38)

Parameters (Units)	Mean ± SD (untransformed data)	
	Test Product-T	Reference Product-R
T_{max} (h)[#]	2.333 (0.500 - 6.000)	2.667 (0.750 - 8.000)
C_{max} (ng/mL)	28.911 ± 6.4872	28.583 ± 6.4883
AUC_{0-t} (ng.h/mL)	602.132 ± 171.1705	595.737 ± 174.8254
$AUC_{0-\infty}$ (ng.h/mL)	641.673 ± 201.0719	637.814 ± 206.7833
λ_z (1/h)	0.045 ± 0.0120	0.046 ± 0.0116
$t_{½}$ (h)	16.424 ± 4.4514	16.159 ± 4.2324
AUC_%Extrap_obs (%)	5.416 ± 3.5481	5.802 ± 3.7261

[#]T_{max} is represented as median (min-max) value.

Table 2. Relative Bioavailability Results for Lorazepam (N = 38)

Parameters	Geometric Least Squares Means			90% Confidence Interval	Intra Subject CV (%)	Power (%)
	Test Product-T	Reference Product-R	Ratio (T/R)%			
lnC_{max}	28.244	27.856	101.4	97.20 - 105.77	10.9	100.0
$lnAUC_{0-t}$	578.646	572.018	101.2	98.58 - 103.80	6.7	100.0
$lnAUC_{0-\infty}$	612.226	607.733	100.7	97.93 - 103.63	7.3	100.0

In accordance with the regulatory requirements, the Test/Reference ratios and their 90% confidence intervals were within the specified limits to show bioequivalence between the test product and the reference product.

As the additional 0.5 mg and 1 mg strengths of the product meet the biowaiver criteria specified in the current bioequivalence guideline, the results and conclusions from the bioequivalence studies on the 2.5 mg product strength can be extrapolated to the other products.

IV.3 Pharmacodynamics

No new pharmacodynamic data have been submitted for these applications and none were required.

IV.4 Clinical efficacy

No new efficacy data have been submitted for these applications and none were required.

IV.5 Clinical safety

With the exception of the safety data submitted with the bioequivalence studies, no new safety data were submitted with these applications.

The safety data from the bioequivalence studies showed that the test and reference products were equally well tolerated. No new or unexpected safety issues were raised from the bioequivalence study.

IV.6 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.

IV.7 Discussion on the clinical aspects

The grant of marketing authorisations was recommended for these applications.

V USER CONSULTATION

A full colour mock-up of the Patient Information Leaflets (PILs) was provided with the application in accordance with legal requirements, including user consultation.

VI OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

The quality of the products is acceptable, and no new non-clinical or clinical safety concerns have been identified. Extensive clinical experience with lorazepam is considered to have demonstrated the therapeutic value of the products. The benefit/risk is, therefore, considered to be positive.

The Summaries of Product Characteristics (SmPCs), Patient Information Leaflet (PIL) and labelling are satisfactory and in line with current guidelines.

In accordance with legal requirements, the current approved versions of the SmPCs and PIL 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 authorisation 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