



Public Assessment Report

National Procedure

Levetiracetam 100mg/ml oral Solution

levetiracetam

PL 55863/0115

Novumgen Limited

LAY SUMMARY

Levetiracetam 100mg/ml oral Solution levetiracetam

This is a summary of the Public Assessment Report (PAR) for Levetiracetam 100mg/ml oral Solution. It explains how this product was assessed and its authorisation recommended, as well as its conditions of use. It is not intended to provide practical advice on how to use this product.

This product will be referred to as Levetiracetam in this lay summary for ease of reading.

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

What is Levetiracetam and what is it used for?

This product is a generic medicine. This means that this medicine is the same as, and considered interchangeable with, a reference medicine already authorised, called Keppra 100mg/ml Oral Solution (PLGB 00039/0772).

Levetiracetam is used:

- on its own in adults and adolescents from 16 years of age with newly diagnosed epilepsy, to treat a certain form of epilepsy. Epilepsy is a condition where the patients have repeated fits (seizures). Levetiracetam is used for the epilepsy form in which the fits initially affect only one side of the brain but could thereafter extend to larger areas on both sides of the brain (partial onset seizure with or without secondary generalisation). Levetiracetam has been given to the patient by their doctor to reduce the number of fits.
- as an add-on to other antiepileptic medicines to treat:
 - partial onset seizures with or without generalisation in adults, adolescents, children and infants from one month of age
 - myoclonic seizures (short, shock-like jerks of a muscle or group of muscles) in adults and adolescents from 12 years of age with juvenile myoclonic epilepsy
 - primary generalised tonic-clonic seizures (major fits, including loss of consciousness) in adults and adolescents from 12 years of age with idiopathic generalised epilepsy (the type of epilepsy that is thought to have a genetic cause)

How does Levetiracetam work?

The active substance, levetiracetam, is an antiepileptic medicine (a medicine used to treat seizures in epilepsy).

How is Levetiracetam used?

The pharmaceutical form of this medicine is an oral solution and the route of administration is oral (by mouth).

Due to the high-level of detail in the usage instructions it is best to refer directly to the PIL and Summaries of Product Characteristics (SmPC) available on the Medicines and Healthcare products Regulatory Agency (MHRA) website, for information on how Levetiracetam is used.

For further information on how Levetiracetam is used, refer to the PIL and Summary of Product Characteristics (SmPC) available on the Medicines and Healthcare products Regulatory Agency (MHRA) website.

This medicine can only be obtained with a prescription.

The patient should always take this medicine exactly as their doctor/pharmacist has told them. The patient should check with their doctor or pharmacist if they are not sure.

What benefits of Levetiracetam have been shown in studies?

Levetiracetam is a generic medicine that fulfils criteria meaning that no additional studies are required. Levetiracetam has been considered a generic medicine of the reference medicine based on a comparison of their physical and chemical characteristics.

What are the possible side effects of Levetiracetam?

For the full list of all side effects reported with this medicine, see Section 4 of the PIL or the SmPC 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 medicine. 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 this medicine.

Because Levetiracetam is a generic medicine, its benefits and possible side effects are considered to be the same as for the reference medicine.

Why was Levetiracetam approved?

It was concluded that, Levetiracetam has been shown to be comparable to the reference medicine. Therefore, the MHRA decided that, as for the reference medicine, the benefits are greater than the risks and recommended that it can be approved for use.

What measures are being taken to ensure the safe and effective use of Levetiracetam?

As for all newly-authorised medicines, a Risk Management Plan (RMP) has been developed for Levetiracetam. The RMP details the important risks of Levetiracetam, how these risks can be minimised, any uncertainties about Levetiracetam (missing information), and how more information will be obtained about the important risks and uncertainties.

The following safety concerns have been recognised for Levetiracetam:

Summary of the Safety Concerns	
Important identified risks	<ul style="list-style-type: none"> • Abnormal behaviour • Blood dyscrasias • Suicidal ideation and behaviour • Suicidality • Seizure Worsening
Important potential risks	<ul style="list-style-type: none"> • None
Missing information	<ul style="list-style-type: none"> • Long term effects on learning, intelligence, growth, endocrine function, puberty and childbearing potential in children with epilepsy or in children exposed in utero • Deterioration of seizure control during pregnancy • Decreased bone mineral density after prolonged levetiracetam exposure

The information included in the SmPC 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 Levetiracetam 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 this application and are satisfactory.

Other information about Levetiracetam

A marketing authorisation for Levetiracetam was granted in the United Kingdom (UK) on 18 June 2025.

The full PAR for Levetiracetam follows this summary.

This summary was last updated in July 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 application for Levetiracetam 100mg/ml oral Solution (PL 55863/0115) could be approved.

The product is approved for the following indications:

As monotherapy in the treatment of partial onset seizures with or without secondary generalisation in adults and adolescents from 16 years of age with newly diagnosed epilepsy.

Levetiracetam is indicated as adjunctive therapy

- in the treatment of partial onset seizures with or without secondary generalisation in adults, adolescents, children and infants from 1 month of age with epilepsy.
- in the treatment of myoclonic seizures in adults and adolescents from 12 years of age with Juvenile Myoclonic Epilepsy.
- in the treatment of primary generalised tonic-clonic seizures in adults and adolescents from 12 years of age with Idiopathic Generalised Epilepsy.

The mechanism of action of levetiracetam still remains to be fully elucidated. *In vitro* and *in vivo* experiments suggest that levetiracetam does not alter basic cell characteristics and normal neurotransmission.

In vitro studies show that levetiracetam affects intraneuronal Ca^{2+} levels by partial inhibition of N-type Ca^{2+} currents and by reducing the release of Ca^{2+} from intraneuronal stores. In addition it partially reverses the reductions in GABA- and glycine-gated currents induced by zinc and β -carbolines.

Furthermore, levetiracetam has been shown in *in vitro* studies to bind to a specific site in rodent brain tissue. This binding site is the synaptic vesicle protein 2A, believed to be involved in vesicle fusion and neurotransmitter exocytosis. Levetiracetam and related analogs show a rank order of affinity for binding to the synaptic vesicle protein 2A which correlates with the potency of their anti-seizure protection in the mouse audiogenic model of epilepsy. This finding suggests that the interaction between levetiracetam and the synaptic vesicle protein 2A seems to contribute to the antiepileptic mechanism of action of the medicinal product.

This application was approved under Regulation 51B of The Human Medicines Regulation 2012, as amended (previously Article 10(1) of Directive 2001/83/EC, as amended), as a generic medicine of a suitable originator medicinal product, Keppra 100mg/ml Oral Solution (PLGB 00039/0772) that has been licensed for a suitable time, in line with the legal requirements.

No new non-clinical studies were conducted, which is acceptable given that the application is for a generic medicinal product of a suitable reference product.

A biowaiver was submitted with this application, which was accepted. No bioequivalence study was required and no new clinical studies were provided with this application.

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

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

A marketing authorisation for Levetiracetam was granted in the United Kingdom (UK) on 18 June 2025.

II QUALITY ASPECTS

II.1 Introduction

The active substance is called levetiracetam. Each ml contains 100 mg of levetiracetam.

The other ingredients are: sodium citrate, citric acid monohydrate, methyl parahydroxybenzoate (E218), ammonium glycyrrhizate, glycerol (E422), maltitol liquid (E965), grape flavour, purified water.

The finished product is packaged in:

The 300 ml glass bottle of Levetiracetam (for children aged 4 years and above, adolescents and adults) is packed in a cardboard box containing a 10 ml oral syringe (graduated every 0.25 ml) and an adaptor for the syringe.

The 150 ml glass bottle of Levetiracetam (for infants and young children aged from 6 months to less than 4 years) is packed in a cardboard box containing a 3 ml oral syringe (graduated every 0.1 ml) and an adaptor for the syringe.

The 150 ml glass bottle of Levetiracetam (for infants aged 1 month to less than 6 months) is packed in a cardboard box containing a 1 ml oral syringe (graduated every 0.05 ml) and an adaptor for the syringe.

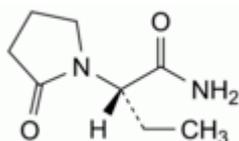
Satisfactory specifications and Certificates of Analysis have been provided for all packaging components. All primary packaging complies with the current regulations concerning materials in contact with food.

II.2 ACTIVE SUBSTANCE

rINN: levetiracetam

Chemical Name: (2S)-2-(2-Oxopyrrolidin-1-yl)butanamide.

Molecular Formula: C₈H₁₄N₂O₂



Chemical Structure:

Molecular Weight: 170.2

Appearance: White or almost white powder.

Solubility: Very soluble in water, soluble in acetonitrile, practically insoluble in heptane.

Levetiracetam 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 PRODUCT

Pharmaceutical development

A satisfactory account of the pharmaceutical development was provided.

Comparative *in vitro* impurity profiles were 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 were provided for all excipients.

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

This product does not contain or consist of genetically modified organisms (GMO).

Manufacture of the product

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

Satisfactory batch formulation data have been provided for the manufacture of the product, 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 18 months, with no special storage conditions, is acceptable.

Shelf-life after first opening: 3 months

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 a marketing authorisation was recommended.

III NON-CLINICAL ASPECTS

III.1 Introduction

As the pharmacodynamic, pharmacokinetic and toxicological properties of levetiracetam 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 this application.

III.3 Pharmacokinetics

No new pharmacokinetic data were provided, and none were required for this application.

III.4 Toxicology

No new toxicology data were provided, and none were required for this application.

III.5 Ecotoxicity/Environmental Risk Assessment

A suitable justification was provided for non-submission of an Environmental Risk Assessment. As the application is for a generic version of an already authorised product, an increase in environmental exposure is not anticipated following approval of the marketing authorisation for the proposed product.

III.6 Discussion on the non-clinical aspects

The grant of a marketing authorisation was recommended.

IV CLINICAL ASPECTS

IV.1 Introduction

The clinical pharmacology, efficacy and safety of levetiracetam is well-known. According to the regulatory requirements, the applicant has provided a suitable biowaiver and a bioequivalence study is not required for this product. An overview based on a literature review is, thus, satisfactory.

IV.2 Pharmacokinetics

No new pharmacokinetic data were submitted for this application and none were required.

IV.3 Pharmacodynamics

No new pharmacodynamic data were submitted for this application and none were required.

IV.4 Clinical efficacy

No new efficacy data were submitted with this application and none were required.

IV.5 Clinical safety

No new safety data were submitted with this application and none were required. The safety profile for this product is considered to be the same as Keppra 100mg/ml Oral Solution (PLGB 00039/0772).

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 a marketing authorisation was recommended for this application.

V USER CONSULTATION

A full colour mock-up of the Patient Information Leaflet (PIL) 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 product is acceptable, and no new non-clinical or clinical safety concerns have been identified. Extensive clinical experience with levetiracetam is considered to have demonstrated the therapeutic value of the compound. The benefit/risk is, therefore,

considered to be positive.

The Summary of Product Characteristics (SmPC), Patient Information Leaflet (PIL) and labelling are satisfactory, in line with current guidelines and consistent with the reference product.

In accordance with legal requirements, the current approved UK version of the SmPC and PIL for this product are available on the MHRA website.

TABLE OF CONTENT OF THE PAR UPDATE

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 SmPC and/or PIL available on the MHRA website.

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