30 March 2023
EMA/216528/2023
Committee for Medicinal Products for Human Use (CHMP)

Assessment report

Lacosamide Adroiq

International non-proprietary name: lacosamide

Procedure No. EMEA/H/C/006047/0000

Note

Assessment report as adopted by the CHMP with all information of a commercially confidential nature deleted.

Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
Address for visits and deliveries Refer to www.ema.europa.eu/how-to-find-us
Send us a question Go to www.ema.europa.eu/contact **Telephone** +31 (0)88 781 6000 An agency of the European Union

Table of contents

List of abbreviations

ADI - acceptable daily intake
Al / Alu – Aluminium
API – Active Pharmaceutical Ingredient
APS – aseptic process simulation
AR – Assessment Report
ASM – Active Substance Manufacturer
ASMF – Active Substance Master File
ASTM - American Society for Testing and Materials
DMF – Drug Master File = Active Substance Master File, ASMF
BCS – Biopharmaceutics Classification System
BE / BEQ – Bioequivalence
BET – bacterial endotoxin test
BSA – bovine serum albumin
BSE/TSE – Bovine Spongiform Encephalopathy / Transmissible Spongiform Encephalopathy
CAS – Chemical Abstracta Services
CCI – Container-closure integrity
CEP – Certificate of Suitability
CFR – Code of Federal Regulations
CFU – colony forming unit
CHMP - Committee for Human Medicine Products
CIP – clean-in-place
C_{max} - maximum plasma Concentration
CMDh - Co-ordination Group for Mutual Recognition and Decentralised procedures - Human
CoA – Certificate of Analysis
COP – clean-out-of-place
CPP's - critical process parameters
CQA – Critical quality attribute
CRS – Chemical reference substances
CU – Content Uniformity
CV – Coefficient of variation
CV - Curriculum Vitae
DAD – diode-array detector
DPM – Drug Product Manufacturer
DSD – droplet-size distribution
EDQM – The European Directorate for the Quality of Medicines & HealthCare
EEA – European Economic Area
EI – Elemental Impurities
ELSD - evaporative light scattering detection
EMA / EMEA – European Medicines Agency
EPAR – European Public Assessment Report
ETFE - ethylenetetrafluoroethylene
EU - European Union
FCC – Food Chemical Codex
FDA – Food and Drug Administration
FPM – Finished Product Manufacturer
FRC - Functionality related characteristics
FTIR – Fourier-transform infrared spectroscopy
FTU – flip-tear-up
GC – Gas Chromatography
GC-MS - Gas chromatography–mass spectrometry
GCP - Good Clinical Practice
GLP - Good Laboratory Practice
GMP – Good Manufacturing Practice
HPLC – High Pressure Liquid Chromatography
HSM – High Shear Mixer
ICDD – International Centre for Diffraction Data
ICH – International Conference on Harmonisation
ICP-MS – Inductively coupled plasma mass spectrometry
INN – International Non-proprietary Name
IPC – In-Process Control
IR – Immediate-release (1), IR – Infrared spectroscopy (2)

IVR(A) – In Vitro Release (Assay)
JP – Japanese Pharmacopoeia
KF – Karl Fisher
LDPE – low density polyethylene
LOD – Loss of drying (1), Limit of Detection (2)
LOQ – Limit of Quantification
LTL - Less-than-lifetime
MAA – Marketing Authorisation Application
MAH - Marketing Authorisation Holder
MDD – Maximum daily dose
MIA – Manufacturing / Importer Authorisation
MS – Mass spectroscopy
MVL - Multivesicular liposomes
N/A – not applicable
NLT – not less than
NMR – Nuclear magnetic resonance spectroscopy
NMT – not more than
OGD – Office of generic drugs
PBS – phosphate buffered saline
PDE – Permitted daily exposure
PE – polyethylene
PES – polyethersulfone
PGI / PGIs – potential genotoxic impurity(ies)
Ph. Eur. – European Pharmacopoeia
PK – pharmacokinetic
PI – Product Information
PP – polypropylene
PPV – Packed Particle Volume
PSD – Particle Size Distribution
(e)PTFE – (expanded) polytetrafluoro-ethylene
PVC – polyvinyl chloride
PVDC – polyvinylidene chloride
QbD – Quality by Design
QC – Quality Control
QOS – Quality Overall Summary
QP – Qualified Person
q.s. – quantity sufficient
RH – Relative Humidity
RMP – reference medicinal product
RRF – Relative Response Factor
RRT – Relative Retention Time
RSD – Relative Standard Deviation
SAL – sterility assurance level
SDS – sodium dodecyl sulfate
SGF – Simulated gastric fluid
SIP – sterilization-in-place (1), steam-in-place (2)
SLS – sodium lauryl sulphate
SmPC / SPC – Summary of Product Characteristics
SOP – steam-out-of-place
TAMC – Total Aerobic Microbial Count
TFF – tangential flow filtration
TLC – Thin Liquid Chromatography
TYMC – Total Combined Yeasts/Moulds Count
USP/NF – United States Pharmacopoeia/National formulary
UV – Ultraviolet
WFI – water for injections
XRD – X-Ray Diffraction

This is a general list of abbreviations. Not all abbreviations are used in this Report

1. Background information on the procedure

1.1. Submission of the dossier

The applicant Extrovis EU Ltd. submitted on 31 March 2022 an application for marketing authorisation to the European Medicines Agency (EMA) for Lacosamide Adroiq, through the centralised procedure under Article 3 (3) of Regulation (EC) No. 726/2004 'Generic of a Centrally authorised product'. The eligibility to the centralised procedure was agreed upon by the EMA/CHMP on 16 December 2021.

The application concerns a generic medicinal product as defined in Article 10(2)(b) of Directive 2001/83/EC and refers to a reference product, as defined in Article 10 (2)(a) of Directive 2001/83/EC, for which a marketing authorisation is or has been granted in the Union on the basis of a complete dossier in accordance with Article 8(3) of Directive 2001/83/EC.

The applicant applied for the following indication:

> Lacosamide Adroiq is indicated as monotherapy in the treatment of partial-onset seizures with or without secondary generalisation in adults, adolescents and children from 2 years of age with epilepsy.
>
> Lacosamide Adroiq is indicated as adjunctive therapy
>
> - in the treatment of partial-onset seizures with or without secondary generalisation in adults, adolescents and children from 2 years of age with epilepsy.
> - in the treatment of primary generalised tonic-clonic seizures in adults, adolescents and children from 4 years of age with idiopathic generalised epilepsy.

1.2. Legal basis, dossier content

The legal basis for this application refers to:

Generic application (Article 10(1) of Directive No 2001/83/EC).

The application submitted is composed of administrative information, complete quality data and literature references instead of non-clinical and clinical data unless justified otherwise.

The chosen reference product is:

Medicinal product which is or has been authorised in accordance with Union provisions in force for not less than 6/8/10 years in the EEA:

- Product name, strength, pharmaceutical form: Vimpat 10 mg/ml solution for infusion
- Marketing authorisation holder: UCB Pharma S.A.
- Date of authorisation: 29 August 2008
- Marketing authorisation granted by Union
- Union Marketing authorisation number: EU/1/08/470/016-017

Medicinal product authorised in the Union/Members State where the application is made or European reference medicinal product:

- Product name, strength, pharmaceutical form: Vimpat 10 mg/ml solution for infusion
- Marketing authorisation holder: UCB Pharma S.A.
- Date of authorisation: 29 August 2008
- Marketing authorisation granted by Union

- Union Marketing authorisation number: EU/1/08/470/016-017

1.3. Information on paediatric requirements

Not applicable.

1.4. Information relating to orphan market exclusivity

1.4.1. Similarity

Pursuant to Article 8 of Regulation (EC) No. 141/2000 and Article 3 of Commission Regulation (EC) No 847/2000, the applicant did not submit a critical report addressing the possible similarity with authorised orphan medicinal products because there is no authorised orphan medicinal product for a condition related to the proposed indication.

1.5. Scientific advice

The applicant did not seek Scientific advice from the CHMP.

1.6. Steps taken for the assessment of the product

The Rapporteur appointed by the CHMP was:

Rapporteur: Selma Arapovic Dzakula

The application was received by the EMA on	31 March 2022
The procedure started on	19 May 2022
The CHMP Rapporteur's first Assessment Report was circulated to all CHMP and PRAC members on	8 August 2022
The PRAC Rapporteur's first Assessment Report was circulated to all PRAC and CHMP members on	19 August 2022
The CHMP agreed on the consolidated List of Questions to be sent to the applicant during the meeting on	15 September 2022
The applicant submitted the responses to the CHMP consolidated List of Questions on	6 December 2022
The CHMP Rapporteur circulated the CHMP and PRAC Rapporteurs Joint Assessment Report on the applicant's responses to the List of Questions to all CHMP members on	30 January 2023
The CHMP agreed on a list of outstanding issues in writing and/or in an oral explanation to be sent to the applicant on	23 February 2023
The applicant submitted the responses to the CHMP List of Outstanding Issues on	27 February 2023

The CHMP Rapporteur circulated the CHMP and PRAC Rapporteurs Joint Assessment Report on the responses to the List of Outstanding Issues to all CHMP and PRAC members on	15 March 2023
The CHMP, in the light of the overall data submitted and the scientific discussion within the Committee, issued a positive opinion for granting a marketing authorisation to Lacosamide Adroiq on	30 March 2023

2. Scientific discussion

2.1. Introduction

This application concerns a generic medicinal product referring to the centrally authorised product Vimpat, which was first authorised in the European Union on 29 August 2008.

The active substance is lacosamide, an amino acid derivate with anticonvulsive activity. Although its mechanism of action has not been fully elucidated, lacosamide has shown to selectively enhance slow inactivation of voltage-gated sodium channels, resulting in stabilization of hyper-excitable neuronal membranes.

The proposed indications for Lacosamide Adroiq are the same as for the reference product: indication as monotherapy in the treatment of partial-onset seizures with or without secondary generalisation in adults, adolescents and children from 2 years of age with epilepsy, as adjunctive therapy for the treatment of partial-onset seizures with or without secondary generalisation in adults, adolescents and children from 2 years of age with epilepsy, and as adjunctive therapy in the treatment of primary generalised tonic-clonic seizures in adults, adolescents and children from 4 years of age with idiopathic generalised epilepsy.

The reference product Vimpat is available as tablets (50mg, 100mg, 150mg, and 200mg), solution for infusion (10mg/mL), and syrup (10mg/mL). Treatment is initiated at a starting dose of 50 mg twice a day which is titrated in weekly increments to a maximum maintenance dose of 200 mg twice a day for adjunctive treatment and 300 mg twice a day for monotherapy. In case of monotherapy, treatment can also be initiated at a starting dose of 100 mg twice a day. Vimpat may be taken with or without food.

The application for Lacosamide Adroiq concerns the solution for infusion (10mg/mL) formulation. Lacosamide Adroiq 10mg/mL solution for infusion contains the same active ingredient in the same concentration as Vimpat solution for infusion (10mg/mL), and Lacosamide Adroiq 10mg/mL solution for infusion is applied for the same indications, strength, and route of administration as the reference product Vimpat. Therefore, in accordance with the Guideline on the Investigation of Bioequivalence (CPMP/EWP/QWP/1401/98), no bioequivalence study was submitted to support the application.

2.2. Quality aspects

2.2.1. Introduction

The finished product is presented as solution for infusion containing 10 mg/mL of lacosamide as active substance.

Other ingredients are water for injections, sodium chloride, and hydrochloric acid (for pH adjustment).

The product is available in type I glass vial with a bromobutyl rubber closure with aluminium flip off seals as described in section 6.5 of the SmPC.

2.2.2. Active substance

General information

The chemical name of the active substance is (2R)-2-Acetamido-N-benzyl-3-methoxypropanamide corresponding to the molecular formula $C_{13}H_{18}N_2O_3$. It has a relative molecular weight of 250.3 and the following structure:

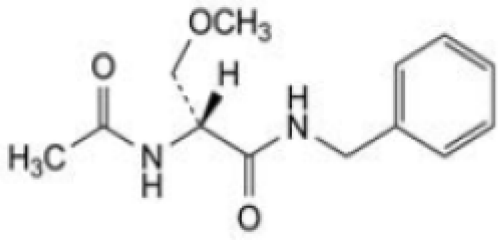

Figure 1: Active substance structure

The chemical structure of the active substance was elucidated solid-state properties confirmed by suitable analytical techniques.

The active substance is a non-hygroscopic white or almost white or light-yellow powder sparingly soluble in water, freely soluble in methanol, practically insoluble in heptane.

Lacosamide contains one chiral centre. Hence it exhibits stereoisomerism.

Manufacture, characterisation and process controls

The active substance is manufactured by one manufacturer.

Detailed information on the manufacturing of the active substance has been provided in the restricted part of the ASMF and it was considered satisfactory.
Adequate in-process controls are applied during the synthesis. The specifications and control methods for intermediate products, starting materials and reagents have been presented.
The characterisation of the active substance and its impurities are in accordance with the EU guideline on chemistry of new active substances.

Detailed discussion on actual and potential impurities that are likely to arise during the synthesis have been provided and the mechanisms utilised for their control are presented.

Potential and actual impurities were well discussed with regards to their origin and characterised.

The active substance is packaged in antistatic polyethylene bags. This is placed inside an outer black polythene bag. Displace the air completely from inner poly bag and tie inner and outer poly bag with a plastic strap. This in turn is enclosed in a HM-HDPE drum and tightly closed which complies with the EC directive 2002/72/EC and EC 10/2011 as amended.

Specification

The active substance specification used by the finished product manufacturer includes tests for appearance (visual), identification (FTIR/Infrared absorption spectroscopy, HPLC), solubility (Ph. Eur.), appearance of solution (Ph. Eur.), water content (Ph. Eur.), sulphated ash / residue of ignition (Ph. Eur.), enantiomeric purity (HPLC), related substances (HPLC), assay (HPLC), impurities (HPLC), residual solvents (GC), dimethyl sulfate content (GCMS), bacterial endotoxins (Ph, Eur.), microbial enumeration (Ph. Eur.).

Proposed specification for lacosamide is in line with the Ph. Eur. monograph. Additional limits set for residual solvents are in line with ICH Q3C and for dimethyl sulfate with ICH M7.
The methods used for the control of the active substance are the same as described in the Ph. Eur. monograph for lacosamide, with exception of the method for related substances and assay.

The analytical methods used have been adequately described and (non-compendial methods) appropriately validated in accordance with the ICH guidelines. Satisfactory information regarding the reference standards used for testing has been presented.

Batch analysis data of two commercial scale batches of the active substance are provided. The results are within the specifications and consistent from batch to batch.

Stability

Stability data from 3 commercial scale batches of active substance from the proposed manufacturer stored in the intended commercial package for up to 60 months under long term conditions (30 ºC / 65% RH) and for up to 6 months under accelerated conditions (40 ºC / 75% RH) according to the ICH guidelines were provided.

All results under long term and accelerated conditions are within proposed limits without significant changes between the testing points.

The stability results indicate that the active substance manufactured by the proposed supplier is sufficiently stable. The stability results justify the proposed retest period of 48 months stored below 30°C in the proposed container.

2.2.3. Finished medicinal product

Description of the product and pharmaceutical development

The finished product is presented as clear, colourless solution free from visible particles.The generic medicinal product has identical qualitative and quantitative composition of the active substance and excipients and the same pharmaceutical form and strength as the reference product Vimpat 10 mg/ml solution for infusion.

The formulation composition is similar to that of the reference medicinal product. Since the finished product is qualitatively and quantitatively similar to the reference medicinal product, the excipients can be considered to be compatible. Additionally, the stability testing of the finished product confirms the compatibility of the excipients. All excipients are well known pharmaceutical ingredients and their quality is compliant with Ph. Eur standards. There are no novel excipients used in the finished product formulation. The list of excipients is included in section 6.1 of the SmPC.

The aim of the formulation development is to develop a generic medicinal product equivalent to the reference medicinal product, to identify and mitigate the risks during the formulation design scale up and to provide control strategy for the manufacturing

No bioequivalence studies have been performed since the product is to be administered as an aqueous intravenous solution containing identical active substance's concentration as the originator and both products contain the same excipients' quantity, in accordance with the Guideline on the investigation of bioequivalence (CPMP/EWP/QWP/1401/98), it is acceptable to exempt bioequivalence studies.

During the manufacturing development, the effect of several Critical Process Parameters (CPPs) were studied to understand their impact on Critical Quality Attributes (CQAs) of the finished product.

The primary packaging is type I glass vial with a bromobutyl rubber closure with aluminum flip off seals. The material complies with Ph. Eur. and EC requirements. The choice of the container closure system has been validated by stability data and is adequate for the intended use of the product.

Manufacture of the product and process controls

The manufacturing process consists of 5 main steps as outlined dispensing, compounding, filtration, filling, terminal sterilization, visual inspection, and packaging. The process is considered to be a standard manufacturing process since it includes terminal sterilisation with the reference Ph. Eur. cycle.

Major steps of the manufacturing process have been validated by a number of studies. It has been demonstrated that the manufacturing process is capable of producing the finished product of intended quality in a reproducible manner. The in-process controls are adequate for this type of manufacturing.

Product specification

The finished product release and shelf-life specifications include appropriate tests for this kind of dosage form: appearance (visual), identification (HPLC, HPLC/PDA-UV), pH (Ph. Eur.), clarity of solution (Ph. Eur.), colour of solution (Ph. Eur.), osmolality (Ph. Eur.), assay (HPLC), related substances (HPLC), container content for injections/extractable volume (Ph. Eur), uniformity of dosage units (Ph. Eur.), visible particles (Ph. Eur.), particulate matter-sub-visible particles (by light obscuration method (Method 1 Test 1.B), bacterial endotoxins (Ph. Eur.), sterility (Ph. Eur.), injections and implanted drug products (Parenteral)-product quality test (Ph. Eur.), container closure integrity test (CCIT) (Ph. Eur.), residual solvents (Ph. Eur.), and elemental impurities.

The provided specification for the finished product includes adequate tests to control the quality of the product. The set specification limits are reasonable and the specified parameters for the finished product are justified in general. The proposed limits for impurities are considered acceptable as they are in line with the Ph. Eur. monograph for Lacosamide infusion.

Risk assessment on the elemental impurities according to ICH Q3D infusion was performed. The assessment examined the sources of elemental impurities and identified several components that had the potential to transfer elemental impurities into finished product. The results obtained show that the content of elemental impurities are below the control threshold.

A risk assessment concerning the potential presence of nitrosamine impurities in the finished product has been performed considering all suspected and actual root causes in line with the "Questions and answers for marketing authorisation holders/applicants on the CHMP Opinion for the Article 5(3) of Regulation (EC) No 726/2004 referral on nitrosamine impurities in human medicinal products" (EMA/409815/2020) and the "Assessment report- Procedure under Article 5(3) of Regulation EC (No)

726/2004- Nitrosamine impurities in human medicinal products" (EMA/369136/2020). Based on the information provided,

The analytical methods used have been adequately described and appropriately validated in accordance with the ICH guidelines.

Batch analysis results are provided for 3 commercial scale batches confirming the consistency of the manufacturing process and its ability to manufacture to the intended product specification.

Stability of the product

Stability data from 3 commercial scale batches of finished product stored for up to 18 months under long term conditions (25°C / 60% RH), and for up to 6 months under accelerated conditions (40°C / 75% RH) according to the ICH guidelines were provided. The batches of the medicinal product are identical to those proposed for marketing and were packed in the primary packaging proposed for marketing.

Samples were tested for appearance, identification, pH, osmolality, clarity of solution, colour of solution, osmolality, assay, related substances, container content for injection, visible particles, particle matter-sub-visible, bacterial endotoxins, sterility, and injections and implanted drug product.

All the results at long-term storage condition of and at accelerated storage condition were found to be well within the limits as per finished product shelf-life specifications.

In addition, one batch was exposed to light as defined in the ICH Guideline on Photostability Testing of New Drug Substances and Products. No significant change is observed during photo stability study for the finished product samples outside immediate pack. All the results were found to be well within the limits. It is concluded that the product is not light sensitive.

Based on available stability data, the proposed shelf-life of 2 years do not store above 25°C as stated in the SmPC (section 6.3) are acceptable.

Adventitious agents

No excipients derived from animal or human origin have been used.

2.2.4. Discussion on chemical, and pharmaceutical aspects

Information on development, manufacture and control of the active substance and finished product has been presented in a satisfactory manner. The results of tests carried out indicate consistency and uniformity of important product quality characteristics, and these in turn lead to the conclusion that the product should have a satisfactory and uniform performance in clinical use.

The applicant has applied QbD principles in the development of the finished product and its manufacturing process. However, no design space was claimed for the manufacturing process of the finished product.

2.2.5. Conclusions on the chemical, pharmaceutical and biological aspects

The quality of this product is considered to be acceptable when used in accordance with the conditions defined in the SmPC. Physicochemical and biological aspects relevant to the uniform clinical performance of the product have been investigated and are controlled in a satisfactory way.

2.2.6. Recommendation for future quality development

Not applicable.

2.3. Non-clinical aspects

2.3.1. Introduction

A non-clinical overview on the pharmacology, pharmacokinetics and toxicology has been provided, which is based on up-to-date and adequate scientific literature. The overview justifies why there is no need to generate additional non-clinical pharmacology, pharmacokinetics and toxicology data. The non-clinical aspects of the SmPC are in line with the SmPC of the reference product.
Ecotoxicity/environmental risk assessment

2.3.2. Ecotoxicity/environmental risk assessment

No Environmental Risk Assessment studies were submitted. This was justified by the applicant as the introduction of Lacosamide Adroiq manufactured by Extrovis EU Ltd. is considered unlikely to result in any significant increase in the combined sales volumes for all lacosamide containing products and the exposure of the environment to the active substance.

In view of data showing an increase of lacosamide consumption over the past years, in accordance with the respective EMA guideline, the applicant agreed to perform a detailed environmental risk assessment (Phase I) as a post-authorisation commitment.

2.3.3. Discussion on non-clinical aspects

A non-clinical overview on the pharmacology, pharmacokinetics and toxicology has been provided, which justifies that there is no need to generate additional non-clinical pharmacology, pharmacokinetics and toxicology data. This is agreed.

The impurity profile of Lacosamide Adroiq 10 mg/mL solution for infusion is discussed and acceptable, thus, additional toxicology studies to qualify the impurity profile of the drug product are not required.

In view of data showing an increase of lacosamide consumption over the past years, in accordance with the respective EMA guideline, the applicant will provide a detailed environmental risk assessment (Phase I) as a post-authorisation measure.

All non-clinical information has been adequately reflected in the SmPC in line with the reference product.

Therefore, the CHMP agrees that Lacosamide Adroiq is approvable from a non-clinical point of view.

2.3.4. Conclusion on the non-clinical aspects

The CHMP considers the non-clinical aspects adequate to support this application.

The CHMP considers the following measures necessary:

- The applicant should perform detailed a Phase I environmental risk assessment for lacosamide.

2.4. Clinical aspects

2.4.1. Introduction

This is an application for solution for infusion containing 10 mg/ml lacosamide. Lacosamide Adroiq contains the same active substance as the reference product Vimpat and is intended for parenteral administration.

The applicant provided a clinical overview outlining the pharmacokinetics and pharmacodynamics as well as efficacy and safety of lacosamide based on published literature. The SmPC is in line with the SmPC of the reference product.

For the clinical assessment the Guideline on the Investigation of Bioequivalence CPMP/EWP/QWP/1401/98) is of particular relevance.

GCP aspect

No new clinical data have been presented.

Exemption

The EMA Guideline on the Investigation of Bioequivalence CPMP/EWP/QWP/1401/98 is of relevance for the clinical assessment. Bioequivalence studies are generally not required if the test product is to be administered as an aqueous intravenous solution containing the same active substance as the currently approved product.

Lacosamide Adroiq 10 mg/ml, solution for infusion, contains the same active ingredient in the same concentration as the reference product Vimpat and for use in the same indication, strength, and route of administration as the reference medicinal product. Therefore, according to the guideline, a bioequivalence study is not considered necessary for the above-mentioned product

2.4.1.1. Post marketing experience

No post-marketing data are available. The medicinal product has not been marketed in any country.

2.4.2. Discussion on clinical aspects

The clinical overview on the clinical pharmacology, efficacy and safety is adequate.

In accordance with the Guideline on the Investigation of Bioequivalence, no bioequivalence study was submitted to support the application.

Lacosamide Adroiq is considered essentially similar to Vimpat 10 mg/l solution for infusion

2.4.3. Conclusions on clinical aspects

Based on scientific literature, a clinical overview has been provided. The overview justifies why there is no need to generate additional clinical data. The clinical aspects of the SmPC are in line with the SmPC of the reference product.

Therefore, the CHMP agreed that no further clinical studies are required.

2.5. Risk Management Plan

2.5.1. Safety concerns

Important Identified Risks	• Cardiac AEs that may be potentially associated with PR interval prolongation or sodium channel modulation
Important Potential Risks	None
Missing Information	• Pregnant or lactating women • Impact on long-term growth, long-term neurodevelopment, and puberty in pediatric population

2.5.2. Pharmacovigilance plan

No additional pharmacovigilance activities.

2.5.3. Risk minimisation measures

None.

2.5.4. Conclusion

The CHMP and PRAC considered that the risk management plan version 1.0 is acceptable.

2.6. Pharmacovigilance

2.6.1. Pharmacovigilance system

The CHMP considered that the pharmacovigilance system summary submitted by the applicant fulfils the requirements of Article 8(3) of Directive 2001/83/EC.

2.6.2. Periodic Safety Update Reports submission requirements

The requirements for submission of periodic safety update reports for this medicinal product are set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and any subsequent updates published on the European medicines web-portal.

2.7. Product information

2.7.1. User consultation

The results of the user consultation with target patient groups on the package leaflet submitted by the applicant show that the package leaflet meets the criteria for readability as set out in the Guideline on the readability of the label and package leaflet of medicinal products for human use.

3. Benefit-risk balance

This application concerns a generic version of lacosamide solution for infusion. The reference product Vimpat is indicated as monotherapy in the treatment of partial-onset seizures with or without secondary generalisation in adults, adolescents and children from 2 years of age with epilepsy. Vimpat is indicated as adjunctive therapy

- in the treatment of partial-onset seizures with or without secondary generalisation in adults, adolescents and children from 2 years of age with epilepsy
- in the treatment of primary generalised tonic-clonic seizures in adults, adolescents and children from 4 years of age with idiopathic generalised epilepsy.

No non-clinical studies have been provided for this application but an adequate summary of the available non-clinical information for the active substance was presented and considered sufficient.

From a clinical perspective, this application does not contain new data on the pharmacokinetics and pharmacodynamics as well as the efficacy and safety of the active substance; the applicant's clinical overview on these clinical aspects based on information from published literature was considered sufficient.

No bioequivalence studies have been provided, which is acceptable and in line with the Guideline on the Investigation of Bioequivalence (CPMP/EWP/QWP/1401/98 Rev. 1/Corr**): bioequivalence studies are generally not required for a parenteral solution, and all conditions are fulfilled. Therefore, the proof of therapeutic equivalence with the reference medicinal product is based on the proof of pharmaceutical equivalence.

A benefit/risk ratio comparable to the reference product can therefore be concluded.

4. Recommendations

Based on the CHMP review of data on quality, safety and efficacy, the CHMP considers by consensus that the benefit-risk balance of Lacosamide Adroiq is favourable in the following indication:

Lacosamide Adroiq is indicated as monotherapy in the treatment of partial-onset seizures with or without secondary generalisation in adults, adolescents and children from 2 years of age with epilepsy. Lacosamide Adroiq is indicated as adjunctive therapy

- in the treatment of partial-onset seizures with or without secondary generalisation in adults, adolescents and children from 2 years of age with epilepsy.
- in the treatment of primary generalised tonic-clonic seizures in adults, adolescents and children from 4 years of age with idiopathic generalised epilepsy.

The CHMP therefore recommends the granting of the marketing authorisation subject to the following conditions:

Conditions or restrictions regarding supply and use

Medicinal product subject to medical prescription.

Other conditions and requirements of the marketing authorisation

- ***Periodic Safety Update Reports***

The requirements for submission of periodic safety update reports for this medicinal product are set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and any subsequent updates published on the European medicines web-portal.

Conditions or restrictions with regard to the safe and effective use of the medicinal product

- **Risk Management Plan (RMP)**

The marketing authorisation holder (MAH) shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the marketing authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:

- At the request of the European Medicines Agency,
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.