LÄKEMEDELSVERKET
SWEDISH MEDICAL PRODUCTS AGENCY

Public Assessment Report
Scientific discussion

Abavalex
(brivaracetam)

SE/H/2536/01-05/DC

This module reflects the scientific discussion for the approval of Abavalex. The procedure was finalised at 2025-08-27. For information on changes after this date please refer to the module 'Update'.

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I. INTRODUCTION

Based on the review of the quality, safety and efficacy data, the Member States have agreed to grant a marketing authorisation for Abavalex, 10 mg, 25 mg, 50 mg, 75 mg, 100 mg, film-coated tablet.

The active substance is brivaracetam. A comprehensive description of the indication and posology is given in the SmPC.

II. EXECUTIVE SUMMARY

II.1 About the product

Mode of action
Brivaracetam displays a high and selective affinity for synaptic vesicle protein 2A (SV2A), a transmembrane glycoprotein found at presynaptic level in neurons and in endocrine cells. Although the exact role of this protein remains to be elucidated it has been shown to modulate exocytosis of neurotransmitters. Binding to SV2A is believed to be the primary mechanism for brivaracetam anticonvulsant activity.

Pharmacotherapeutic group: antiepileptics, other antiepileptics, ATC code: N03AX23.

Claimed indication
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.

II.2 General comments on the submitted dossier

The application for Abavalex, 10 mg, 25 mg, 50 mg, 75 mg, 100 mg, film-coated tablet, is a Generic Art. 10(1) application submitted according to Directive 2001/83/EC. The applicant applies through the Decentralised Procedure with Sweden acting as reference member state (RMS) and AT, BG, CZ, DE, DK, HU, PL, RO and SK as concerned member states (CMS).

The reference medicinal product chosen for the purposes of establishing the expiry of the data protection period is Briviact, 100 mg, film-coated tablet, authorised in in the Union since 2016, with with UCB Pharma S.A. as marketing authorisation holder.

The reference product used in the bioequivalence study is Briviact, 100 mg, film-coated tablet from the Austrian market with UCB Pharma S.A. as marketing authorisation holder.

II.3 General comments on compliance with GMP, GLP, GCP and agreed ethical principles

The RMS has been assured that acceptable standards of GMP are in place for these product types at all sites responsible for the manufacture and assembly of this product.

For manufacturing sites within the Community, the RMS has accepted copies of current manufacturer authorisations issued by inspection services of the competent authorities as certification that acceptable standards of GMP are in place at those sites.

GMP active substance
Regarding the statement on GMP for the active substance a statement/declaration is provided from the manufacturer(s) responsible for manufacture of the finished product and batch release situated in the EU.

GCP
A statement on the application of appropriate GCP standards in the submitted study has been provided.

The bioanalytical facility was inspected by the DE authority in 2025, without any critical findings. The clinical site has not been inspected. However, based on the submitted audit reports, there are no direct reason for rejection of the data.

III. SCIENTIFIC OVERVIEW AND DISCUSSION

III.1 Quality aspects

Drug substance
The structure of the drug substance has been adequately proven, and its physico-chemical properties are sufficiently described.

The manufacture of the drug substance has been adequately described, and satisfactory specifications have been provided for starting materials, reagents and solvents.

The drug substance specification includes relevant tests and the limits for impurities and degradation products have been justified. The analytical methods applied are suitably described and validated.

Stability studies confirm the retest period.

Drug Product
The medicinal product is formulated using excipients listed in section 6.1 in the Summary of Product Characteristics.

The manufacturing process has been sufficiently described and critical steps identified.

The tests and limits in the specification are considered appropriate to control the quality of the finished product in relation to its intended purpose.

Stability studies have been performed and data presented support the shelf life and special precautions for storage claimed in the Summary of Product Characteristics, sections 6.3 and 6.4.

III.2 Non-clinical aspects

Pharmacology/Pharmacokinetics/Toxicology
Pharmacodynamic, pharmacokinetic and toxicological properties of brivaracetam are well known. As brivaracetam is a widely used, well-known active substance, no further studies are required, nor does the applicant provide any. Overview based on literature review is, thus, appropriate.

Environmental Risk Assessment (ERA)
Since Abavalex is a generic product, it will not lead to an increased exposure to the environment. An

environmental risk assessment is therefore not deemed necessary.

There are no objections to approval of Abavalex from a non-clinical point of view.

III.3 Clinical aspects

Pharmacokinetics
To support the marketing authorisation application the applicant has conducted one bioequivalence study comparing Abavalex, 100 mg, film coated tablets with the reference product Briviact, 100 mg, film coated tablets.

Pharmacokinetic properties of the active substance
Absorption: Brivaracetam is rapidly and completely absorbed after oral administration and the absolute bioavailability is approximately 100 %. Following an oral dose of Brivaracetam without food maximal plasma concentrations occur at approximately 1 hour (t_{max} range is 0.25 to 3 h). Coadministration with a high-fat meal slowed down the absorption rate (median t_{max} 3 h) and decreased the maximum plasma concentration (37 % lower) of brivaracetam, while the extent of absorption remained unchanged.

The pharmacokinetics of Brivaracetamis not affected by food, and therefore there are no restrictions with respect to food in the SmPC of the originator.

Linearity: The pharmacokinetics of Brivaracetamis linear within the dose range 10 to at least 600 mg.

Elimination: The terminal half-life is approximately 9 hours.

Study 002B23
Methods
This was a single-dose, two-way crossover study conducted in 30 healthy volunteers, comparing Abavalex, 100 mg, film coated tablets with the reference product Briviact, 100 mg, film coated tablets under fasting conditions. Blood samples for concentration analysis were collected pre-dose and up to 48 hours post-dose. Plasma concentrations of brivaracetam were determined with an LC-MS/MS method. Analysis of variance (ANOVA) was performed on the ln-transformed data for AUC_{0-t} and C_{max}. The study was conducted between 6th September 2023 and 21st September 2023.

Results
The results from the pharmacokinetic and statistical analysis are presented in Table 1 below.

Table 1. Pharmacokinetic parameters (non-transformed values; arithmetic mean ± SD, t_{max} median, range) for brivaracetam, n=30.

Treatment	AUC_{0-t} ng*h/ml	C_{max} ng/ml	t_{max} h
Test	**31801 ± 5149**	**2892 ± 723**	**0.75 (0.33- 3.00)**
Reference	**31668.54 ± 5225.083**	**2815.52 ± 652.597**	**0.75 (0.33-2.50)**
***Ratio (90% CI)**	**100.50 (99.45 - 101.55)**	**102.32 (97.65- 107.20)**	**-**
AUC_{0-t} area under the plasma concentration-time curve from time zero to t hours C_{max} maximum plasma concentration t_{max} time for maximum plasma concentration			

**calculated based on ln-transformed data*

For AUC_{0-t} and C_{max} the 90% confidence interval for the ratio of the test and reference products fell within the conventional acceptance range of 80.00-125.00%.

A biowaiver was sought for the additional strengths 10 mg, 25 mg, 50 mg and 75 mg.

Discussion and overall conclusion

The bioequivalence study and its statistical evaluation were in accordance with accepted standards for bioequivalence testing, as stated in the Guideline on the investigation of bioequivalence (CPMP/EWP/QWP/1401/98 Rev 1/Corr). The bioanalytical methods were adequately validated.

Based on the submitted bioequivalence study, brivaracetam, 100 mg, tablets are considered bioequivalent with Abavalex, 100 mg, tablets.

The results of study 002B23 with 100 mg formulation can be extrapolated to other strengths 10 mg, 25 mg, 50 mg and 75 mg.

Pharmacodynamics/Clinical efficacy/Clinical safety

No new studies on pharmacodynamics, clinical efficacy or clinical safety have been submitted. Provided that bioequivalence with the originator product is demonstrated, additional data is not necessary.

Pharmacovigilance system

Proposed MAH : G.L. Pharma GmbH

The Applicant has submitted a signed Summary of the Applicant's/Proposed Future MAH's Pharmacovigilance System. Provided that the Pharmacovigilance System Master File fully complies with the new legal requirements as set out in the Commission Implementing Regulation and as detailed in the GVP module, the RMS considers the Summary acceptable.

Risk Management Plan

The MAH has submitted a risk management plan, in accordance with the requirements of Directive 2001/83/EC as amended, describing the pharmacovigilance activities and interventions designed to identify, characterise, prevent or minimise risks relating to Abavalex.

Part II Safety specification
The MAH has submitted the version 0.2 RMP dated 2025-02-06 and proposed the following summary safety concerns:

Summary of safety concerns	
Important identified risks	- Suicidality (class label for anticonvulsant products)
Important potential risks	- None
Missing information	- Data during pregnancy and lactation - Long-term effects on growth, endocrine function or sexual maturation, neurodevelopment, and cognitive and psychomotor development in paediatric patients

Having considered the data in the safety specification the assessor agrees that the safety concerns listed by the MAH are appropriate as the safety concerns are aligned with the RMP version 8.1 for the reference product.

Part III Pharmacovigilance Plan
Routine pharmacovigilance is suggested.
The Applicant propose routine pharmacovigilance activities beyond adverse reactions reporting and signal detection in form of specific adverse drug reaction follow-up forms concerning use during pregnancy (pregnancy report form), which is acknowledged and endorsed (even though not specified in the RMP for the reference medicinal product).
Furthermore, the Applicant also suggest, to participate in the EURAP registry by encouraging prescribers to register pregnant women exposed to antiepileptic drugs into the EURAP registry, as applicable. This will be warranted via the specific adverse reaction follow-up form mentioned above. This is according to PRAC advice (PRAC meeting 2-5 September 2024) and is endorsed.

No additional pharmacovigilance activities are proposed by the applicant, which is endorsed.

Part V Risk minimisation measures
Routine risk minimisation is suggested, and no additional risk minimisation activities are proposed by the applicant, which is endorsed.

Part VI Summary of the RMP
The Summary of the RMP is endorsed

Conclusion RMP assessment
The submitted Risk Management Plan, version 0.2 signed 2025-02-06 is considered acceptable.

The 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 RMS;
- 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.

If the dates for submission of a PSUR and the update of a RMP coincide, they can be submitted at the same time, but via different procedures.

Periodic Safety Update Report (PSUR)
Active substance is currently listed in the published EURD list

With regard to PSUR submission, the MAH should take the following into account:

- PSURs shall be submitted in accordance with the requirements set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and published on the European medicines web-portal. Marketing authorisation holders shall continuously check the European medicines web-portal for the DLP and frequency of submission of the next PSUR.

- For medicinal products authorized under the legal basis of Article 10(1) or Article 10a of Directive 2001/83/EC, no routine PSURs need to be submitted, unless otherwise specified in the EURD list.

- In case the active substance will be removed in the future from the EURD list because the MAs have been withdrawn in all but one MS, the MAH shall contact that MS and propose DLP and frequency for further PSUR submissions together with a justification.

Common renewal date
The common renewal date will be 5 years after closure of the DCP.

IV. BENEFIT RISK ASSESSMENT

The quality of the generic product, Abavalex, is found adequate. There are no objections to approval of Abavalex, from a non-clinical and clinical point of view. Bioequivalence between the test and reference product has been adequately demonstrated. The product information is acceptable. The benefit/risk is considered positive, and the application is therefore recommended for approval.

V. RECOMMENDATIONS AND CONDITIONS FOR MARKETING AUTHORISATION AND PRODUCT INFORMATION

V.1 List of recommendations not falling under Article 21a/22 of Directive 2001/83/EC

Post approval commitments
N/A

V.2 List of conditions pursuant to Article 21a or specific obligations pursuant to Article 22 of Directive 2001/83/EC

- **Additional risk minimisation measures (including educational material)**

N/A.

- **Obligation to conduct post-authorisation measures in accordance with Article 21a of Directive 2001/83/EC**

N/A.

- **Specific obligation to complete post-authorisation measures for the marketing authorisation under Exceptional circumstances in accordance with Article 22 of Directive 2001/83/EC**

N/A.

V.3 Summary of Product Characteristics (SmPC)

The approved SmPC is available in the MRI Product Index.

V.4 Package Leaflet (PL)

V.4.1 Package Leaflet

The approved PL is available in the MRI Product Index.

V.4.2 Assessment of User Testing

The package leaflet has been evaluated via a user consultation study in accordance with the requirements of Articles 59(3) and 61(1) of Directive 2001/83/EC. The language used for the purpose of user testing the PL was English.
The results 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.

V.5 Labelling

The approved Labelling is available in the MRI Product Index.

VI. STEPS TAKEN AFTER THE FINALISATION OF THE INITIAL PROCEDURE - SUMMARY

Procedure number	Scope	Product Information affected (Yes/No)	Date of end of procedure	Approval/ non approval	Summary/ Justification for refuse
-	-	-	-	-	-