

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

PRODUCTS SUBJECT TO MEDICAL PRESCRIPTION)

1. Name of medicinal product

BRIVARACETAM Tablets 50 mg

2. Qualitative and Quantitative Composition

Each film coated tablet contains:

BRIVARACETAM 50 mg

Excipients Q.S.

Colour: Red Oxide of Iron, Yellow oxide of iron and Titanium dioxide

3. Pharmaceutical Form:

Tablet

4. Clinical Particulars

4.1 Indication

It 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.

4.2 Posology and Administration:

The physician should prescribe the most appropriate formulation and strength according to weight and dose.

The recommended posology for adults, adolescents and children from 2 years of age is summarised in the following table. The dose should be administered in two equally divided doses, approximately 12 hours apart.

The recommended starting dose is either 50 mg/day or 100 mg/day based on physician's assessment of required seizure reduction versus potential side effects. Based on individual patient response and tolerability, the dose may be adjusted in the effective dose range of 50 mg/day to 200 mg/day.

Method of administration

Brivaracetam film-coated tablets must be taken orally and swallowed in whole with liquid and may be taken with or without food. Patients not being able to swallow tablets in whole or patients for whom the dose can not be met with the use of whole tablets should use Briviact 10 mg/ml oral solution.

4.3. Contraindication

Hypersensitivity to the active substance or other pyrrolidone derivatives or to any of the excipients.

4.4 Special Warning & precautions for use

Suicidal ideation and behaviour

Suicidal ideation and behaviour have been reported in patients treated with anti-epileptic drugs (AEDs), including brivaracetam, in several indications. A meta-analysis of randomized placebocontrolled clinical studies of AEDs has also shown a small increased risk of suicidal ideation and behaviour. The mechanism of this risk is not known and the available data do not exclude the possibility of an increased risk for brivaracetam.

Patients should be monitored for signs of suicidal ideation and behaviours and appropriate treatment should be considered. Patients (and caregivers of patients) should be advised to seek medical advice should any signs of suicidal ideation or behaviour emerge. See also section 4.8, paediatric data.

Excipients

Lactose intolerance

Brivaracetam film-coated tablets contain lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

Sodium content

Brivaracetam film-coated tablets contain less than 1 mmol sodium (23mg) per tablet, that is to say essentially 'sodium free'.

4.5. Interaction with other medicinal products and other forms of interaction

Pharmacodynamic interactions

Concomitant treatment with levetiracetam

In the clinical studies, although the numbers were limited, there was no observed benefit of brivaracetam versus placebo in patients taking levetiracetam concurrently. No additional safety or tolerability concern was observed.

Interaction with alcohol

In a pharmacokinetic and pharmacodynamic interaction study between brivaracetam 200 mg single dose and ethanol 0.6 g/L continuous infusion in healthy subjects, there was no pharmacokinetic interaction, but brivaracetam approximately doubled the effect of alcohol on psychomotor function, attention and memory. Intake of brivaracetam with alcohol is not recommended.

Pharmacokinetic interactions

Effects of other medicinal products on the pharmacokinetics of brivaracetam. The main disposition pathway of brivaracetam is by CYP-independent hydrolysis. A second disposition pathway involves hydroxylation mediated by CYP2C19.

Brivaracetam plasma concentrations may increase when coadministered with CYP2C19 strong inhibitors (e.g. fluconazole, fluvoxamine), but the risk of a clinically relevant CYP2C19-mediated interaction is considered to be low. Limited clinical data are available implying that coadministration of cannabidiol may increase the plasma exposure of brivaracetam, possibly through CYP2C19 inhibition, but the clinical relevance is uncertain.

Strong enzyme inducing AEDs

Brivaracetam plasma concentrations are decreased when coadministered with strong enzyme inducing AEDs (carbamazepine, phenobarbital, phenytoin) but no dose adjustment is required. Other enzyme inducers

Other strong enzyme inducers (such as St John's wort (*Hypericum perforatum*)) may also decrease the systemic exposure of brivaracetam. Therefore, starting or ending treatment with St John's wort should be done with caution.

Effects of brivaracetam on other medicinal products

Brivaracetam given 50 or 150 mg/day did not affect the AUC of midazolam (metabolised by CYP3A4). The risk of clinically relevant CYP3A4 interactions is considered to be low.

Oral contraceptives

Co-administration of brivaracetam (100 mg/day) with an oral contraceptive containing ethinylestradiol (0.03 mg) and levonorgestrel (0.15 mg) did not influence the pharmacokinetics of either substance. When brivaracetam was coadministered at a dose of 400 mg/day (twice the recommended maximum daily dose) with an oral contraceptive containing ethinylestradiol (0.03 mg) and levonorgestrel (0.15 mg), a reduction in oestrogen and progestin AUCs of 27 % and 23 %, respectively, was observed without impact on suppression of ovulation. There was generally no change in the concentration-time profiles of the endogenous markers estradiol, progesterone, luteinizing hormone (LH), follicle stimulating hormone (FSH), and sex hormone binding globulin (SHBG).

4.6 Fertility, Pregnancy, and lactation

If a woman decides to become pregnant, the use of brivaracetam should be carefully reevaluated.

Brivaracetam is excreted in human breast milk. A decision should be made whether to discontinue breastfeeding or to discontinue brivaracetam, taking into account the benefit of the medicinal product to the mother. In case of co-administration of brivaracetam and carbamazepine, the amount of carbamazepine-epoxide excreted in breast milk could increase.

4.7. Effects on ability to drive and use machines

Brivaracetam has minor or moderate influence on the ability to drive and use machines.

Due to possible differences in individual sensitivity some patients might experience somnolence, dizziness, and other central nervous system (CNS) related symptoms. Patients should be advised not to drive a car or to operate other potentially hazardous machines until they are familiar with the effects of brivaracetam on their ability to perform such activities.

4.8. Undesirable effects

The most commonly observed adverse events are somnolence, dizziness, Nausea, nausea, vertigo, balance disorder, anxiety, fatigue, irritability, aggression, insomnia, depression, and suicidal ideation.

Reporting of suspected adverse reactions

Health care professionals are asked to report any suspected adverse reactions via the <https://pv.pharmacyboardkenya.org>

4.9. Overdose

Symptoms

Somnolence and dizziness have been reported in a healthy subject taking a single dose of 1,400 mg of brivaracetam.

The following adverse reactions were reported with brivaracetam overdose: nausea, vertigo, balance disorder, anxiety, fatigue, irritability, aggression, insomnia, depression, and suicidal ideation in the post-marketing experience. In general, the adverse reactions associated with brivaracetam overdose were consistent with the known adverse reactions.

Management of overdose

There is no specific antidote for overdose with brivaracetam. Treatment of an overdose should include general supportive measures. Since less than 10 % of brivaracetam is excreted in urine, haemodialysis is not expected to significantly enhance brivaracetam clearance

5. Pharmacological properties

5.1. Pharmacodynamic properties

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

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.

5.2. Pharmacokinetic Properties

Brivaracetam film-coated tablets, oral solution and solution for intravenous injection show the same AUC, while the maximum plasma concentration is slightly higher after intravenous administration. Brivaracetam exhibits linear and time-independent pharmacokinetics with low intra- and inter-subject variability, and features complete absorption, very low protein binding, renal excretion following extensive biotransformation, and pharmacologically inactive metabolites.

Absorption

Brivaracetam is rapidly and completely absorbed after oral administration and the absolute bioavailability is approximately 100 %. The median t_{max} for tablets taken without food is 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.

Distribution

Brivaracetam is weakly bound (≤ 20 %) to plasma proteins. The volume of distribution is 0.5 L/kg, a value close to that of the total body water.

Due to its lipophilicity (Log P) brivaracetam has high cell membrane permeability.

Biotransformation

Brivaracetam is primarily metabolized by hydrolysis of the amide moiety to form the corresponding carboxylic acid (approximately 60 % the elimination), and secondarily by hydroxylation on the propyl side chain (approximately 30 % the elimination). The hydrolysis of the amide moiety leading to the carboxylic acid metabolite (34 % of the dose in urine) is supported by hepatic and extra-hepatic amidase. In vitro, the hydroxylation of brivaracetam is mediated primarily by CYP2C19. Both metabolites, are further metabolised forming a common hydroxylated acid formed predominantly by hydroxylation of the propyl side chain on the carboxylic acid metabolite (mainly by CYP2C9). In vivo, in human subjects possessing ineffective mutations of CYP2C19, production of the hydroxy metabolite is decreased 10-fold while brivaracetam itself is increased by 22 % or 42 % in individuals with one or both mutated alleles. The three metabolites are not pharmacologically active.

Elimination

Brivaracetam is eliminated primarily by metabolism and by excretion in the urine. More than 95 % of the dose, including metabolites, is excreted in the urine within 72 hours after intake. Less than 1 % of the dose is excreted in faeces and less than 10 % of brivaracetam is excreted unchanged in urine. The terminal plasma half-life (t_{1/2}) is approximately 9 hours. The total plasma clearance in patients was estimated to 3.6 L/h.

5.3. Preclinical Safety Data

Not Applicable

6. pharmaceutical Particulars

6.1. List of Excipients

Microcrystalline Cellulose

Starch

Lactose

Sodium starch glycolate

PVPK 30

Isopropyl alcohol

Magnesium stearate

Talc croscarmellose sodium

Colloidal silicon dioxide

Yellow oxide of iron

Red oxide of iron

Titanium Dioxide

6.2. Incompatibilities

Not Applicable

6.3. Shelf Life

3 years (36 months)

6.4. special precaution for storage

Do not store above 30°C.

Keep out of reach of children.

Store below 30°C.

6.5. Nature and contents of container

100 Tablets in a Alu / Alu. Each Blister in a Printed Box with Pack Insert.

6.6. Special precautions for disposal

Not applicable

7. MARKETING AUTHORISATION HOLDER

REDEFINE HEALTHCARE LIMITED

3 RD FLOOR,CORNER PLAZA,WESTLANDS,

P.O BOX 1907-00606 NAIROBI

8. MARKETING AUTHORISATION NUMBER(S)

H2025/CTD11809/25938

**9. DATE OF FIRST AUTHORISATION / RENEWAL OF THE
AUTHORISATION**

Date of first authorisation: 08.07.2025

10. DATE OF REVISION OF THE TEXT

08.07.2025