Front

Brivatam

(B r i v a r a c e t a m)

Tablet, Oral Solution & Injection

بریواٹیم

COMPOSITION:

Brivatam Tablet 25 mg:
Each film coated tablet contains:
Brivaracetam ..... 25 mg.

Product Specs.: Innovator

Brivatam Tablet 50 mg:
Each film coated tablet contains:
Brivaracetam ..... 50 mg.

Product Specs.: Innovator

Brivatam Tablet 100 mg:
Each film coated tablet contains:
Brivaracetam ..... 100 mg.

Product Specs.: Innovator

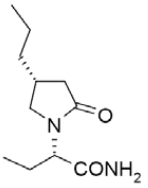
Brivatam Oral Solution 10 mg/ml:
Each ml contains:
Brivaracetam ..... 10 mg.

Product Specs.: Innovator

Brivatam Injection 50 mg/5 ml:
Each 5 ml ampoule contains:
Brivaracetam ..... 50 mg.

Product Specs.: Innovator

DESCRIPTION:
Brivaracetam is an orally bioavailable levetiracetam derivative, with anticonvulsant activity. Although the exact mechanism through which Brivaracetam exerts its effects is not fully known, this agent targets and binds to synaptic vesicle protein 2A (SV2A) in the brain. This prevents synaptic vesicle exocytosis and the synaptic release of certain, as of yet not fully known, excitatory neurotransmitters. This may inhibit impulse conduction across synapses, decrease neuronal (hyper-)excitability, and may modulate epileptogenesis. SV2A, a membrane glycoprotein present in neuronal synaptic vesicles, plays a key role in action potential-induced neurotransmitter release in the brain.
Brivaracetam is a DEA Schedule V controlled substance. Substances in the DEA Schedule V have a low potential for abuse relative to substances listed in Schedule IV and consist primarily of preparations containing limited quantities of certain narcotics.
Brivaracetam is a relatively unique anticonvulsant that is typically used in combination with other antiepileptic medications for partial onset seizures. Brivaracetam has been linked to rare instances of serum aminotransferase and alkaline phosphatase elevations during treatment and is suspected of causing rare cases of clinically apparent drug induced liver disease.



Mechanism of Action:
The exact mechanism by which Brivaracetam produces anticonvulsant activity is not known. Anticonvulsant activity may reside in modulation of synaptic vesicle protein 2A (SV2A) function in the brain. Brivaracetam has highly selective and reversible affinity for SV2A, occupying 80 to 90% of SV2A within 5 to 15 minutes at clinically relevant doses, which represents maximal seizure protection in animal models. Brivaracetam has a 15- to 30-fold higher affinity for SV2A compared to levetiracetam. Additional anticonvulsant activity may be related to the modulation of voltage-dependent sodium channels.

CLINICAL PHARMACOLOGY:
Pharmacokinetics:
Brivaracetam is administered orally and intravenously. Protein binding is approximately 20% or less. Brivaracetam is primarily metabolized by hydrolysis of the amide moiety to form a carboxylic acid metabolite and secondarily by CYP2C19 mediated hydroxylation on the propyl side chain to form a hydroxy metabolite. An additional hydroxy acid metabolite is formed by hydrolysis of the amide moiety on the hydroxy metabolite or hydroxylation of the propyl side chain on the carboxylic acid metabolite. None of the 3 metabolites are pharmacologically active. Genetic variations in CYP2C19 may influence Brivaracetam blood concentrations, as increases of 22% and 42% have been observed in individuals with one or both mutated alleles. Brivaracetam is excreted renally with less than 10% excreted unchanged in the urine. Fecal excretion accounts for less than 1% of the dose. Brivaracetam plasma half-life is approximately 9 hours. Brivaracetam oral tablets, oral solution, and intravenous injection may be used interchangeably.
Affected cytochrome P450 isoenzymes:
CYP2C19. Brivaracetam is metabolized by CYP2C19. A drug interaction study with rifampin demonstrated a 45% decrease in Brivaracetam plasma concentrations, likely secondary to CYP2C19 induction. Concomitant administration with CYP inhibitors or transporter inhibitors is unlikely to significantly influence Brivaracetam exposure.

INDICATIONS:
Brivaracetam is indicated as adjunctive therapy in the treatment of partial-onset seizures with or without secondary generalization in adult and adolescent patients from 16 years of age with epilepsy.

DOSAGE AND ADMINISTRATION:
Oral dosage:
Adults: 50 mg PO twice daily. Adjust dosage to 25 to 100 mg PO twice daily based on clinical response and tolerability.
Adolescents 16 to 17 years: 50 mg PO twice daily. Adjust dosage to 25 to 100 mg PO twice daily based on clinical response and tolerability.
Children and Adolescents younger than 16 years weighing 50 kg or more: 25 to 50 mg PO twice daily. Adjust dosage up to 100 mg PO twice daily based on clinical response and tolerability.
Children and Adolescents younger than 16 years weighing 20 to 49 kg: 0.5 to 1 mg/kg/dose PO twice daily. Adjust dosage up to 2 mg/kg/dose PO twice daily based on clinical response and tolerability.
Infants and Children weighing 11 to 19 kg: 0.5 to 1.25 mg/kg/dose PO twice daily. Adjust dosage up to 2.5 mg/kg/dose PO twice daily based on clinical response and tolerability.
Infants and Children weighing less than 11 kg: 0.75 to 1.5 mg/kg/dose PO twice daily. Adjust dosage up to 3 mg/kg/dose PO twice daily based on clinical response and tolerability.
Oral Solution:
10 mg/mL: slightly viscous, clear, colorless to yellowish, raspberry-flavored liquid. Injection 50 mg in 5 mL in one single-dose injection. It is a clear, colorless, sterile solution.
Intravenous dosage:
Adults: 50 mg IV twice daily. Adjust dosage to 25 to 100 mg IV twice daily based on clinical response and tolerability. Use IV route when oral administration is temporarily not feasible. IV therapy beyond 4 consecutive days has not been evaluated in clinical trials.

Adolescents 16 to 17 years: 50 mg IV twice daily. Adjust dosage to 25 to 100 mg IV twice daily based on clinical response and tolerability. Use IV route when oral administration is temporarily not feasible. IV therapy beyond 4 consecutive days has not been evaluated in clinical trials.
Children and Adolescents younger than 16 years weighing 50 kg or more: 25 to 50 mg IV twice daily. Adjust dosage up to 100 mg IV twice daily based on clinical response and tolerability. Use IV route when oral administration is temporarily not feasible. IV therapy beyond 4 consecutive days has not been evaluated in clinical trials.
Children and Adolescents younger than 16 years weighing 20 to 49 kg: 0.5 to 1 mg/kg/dose IV twice daily. Adjust dosage up to 2 mg/kg/dose IV twice daily based on clinical response and tolerability. Use IV route when oral administration is temporarily not feasible. IV therapy beyond 4 consecutive days has not been evaluated in clinical trials.
Infants and Children weighing 11 to 19 kg: 0.5 to 1.25 mg/kg/dose IV twice daily. Adjust dosage up to 2.5 mg/kg/dose IV twice daily based on clinical response and tolerability. Use IV route when oral administration is temporarily not feasible. IV therapy beyond 4 consecutive days has not been evaluated in clinical trials.
Infants and Children weighing less than 11 kg: 0.75 to 1.5 mg/kg/dose IV twice daily. Adjust dosage up to 3 mg/kg/dose IV twice daily based on clinical response and tolerability. Use IV route when oral administration is temporarily not feasible. IV therapy beyond 4 consecutive days has not been evaluated in clinical trials.

WARNINGS & PRECAUTIONS:
Suicidal behavior:
Ideation Antiepileptic drugs (AEDs), including Brivaracetam, increase the risk of suicidal thoughts or behavior in patients taking these drugs for any indication. Patients treated with any AED for any indication should be monitored for the emergence or worsening of depression, suicidal thoughts or behavior, and/or any unusual changes in mood or behavior.
Anyone considering prescribing Brivaracetam or any other AED must balance the risk of suicidal thoughts or behaviors with the risk of untreated illness. Epilepsy and many other illnesses for which AEDs are prescribed are themselves associated with morbidity and mortality and an increased risk of suicidal thoughts and behavior. Should suicidal thoughts and behavior emerge during treatment, consider whether the emergence of these symptoms in any given patient may be related to the illness being treated.
Neurological adverse reactions:
Brivaracetam causes somnolence, fatigue, dizziness, and disturbance in coordination. Patients should be monitored for these signs and symptoms and advised not to drive or operate machinery until they have gained sufficient experience on Brivaracetam to gauge whether it adversely affects their ability to drive or operate machinery. Somnolence and Fatigue Brivaracetam causes dose-dependent increases in somnolence and fatigue-related adverse reactions (fatigue, asthenia, malaise, hypersomnia, sedation, and lethargy). Dizziness and Disturbance in Gait and Coordination Brivaracetam causes adverse reactions related to dizziness and disturbance in gait and coordination (dizziness, vertigo, balance disorder, ataxia, nystagmus, gait disturbance, and abnormal coordination).
Psychiatric adverse reactions:
Psychiatric events include both non-psychotic symptoms (irritability, anxiety, nervousness, aggression, belligerence, anger, agitation, restlessness, depression, depressed mood, tearfulness, apathy, altered mood, mood swings, affect lability, psychomotor hyperactivity, abnormal behavior, and adjustment disorder) and psychotic symptoms (psychotic disorder along with hallucination, paranoia, acute psychosis, and psychotic behavior).
Hypersensitivity:
Bronchospasm and Angioedema Brivaracetam can cause hypersensitivity reactions. Bronchospasm and angioedema have been reported in patients taking Brivaracetam. If a patient develops hypersensitivity reactions after treatment with Brivaracetam, the drug should be discontinued.
Withdrawal of antiepileptic:
As with most antiepileptic drugs, Brivaracetam should generally be withdrawn gradually because of the risk of increased seizure frequency and status epilepticus. But if withdrawal is needed because of a serious adverse event, rapid discontinuation can be considered.

ADVERSE REACTIONS:
The following serious adverse reactions are described elsewhere in labeling:
- Suicidal Behaviour and Ideation [see Warnings and Precautions]
- Neurological Adverse Reactions [see Warnings and Precautions]
- Psychiatric Adverse Reactions [see Warnings and Precautions]
- Hypersensitivity: Bronchospasm and Angioedema [see Warnings and Precautions]
- Withdrawal of Antiepileptic Drugs [see Warnings and Precautions]

SPECIAL POPULATIONS:
Pregnancy:
There are no adequate and well-controlled studies in pregnant women.
Nursing mothers:
It is not known whether Brivaracetam is excreted in human milk. Because many drugs are excreted into human milk, a decision should be made whether to discontinue nursing or to discontinue Brivaracetam, taking into account the importance of the drug to the mother.
Pediatric use:
Safety and effectiveness of Brivaracetam in adolescents 16 years of age have been established. Safety and effectiveness of Brivaracetam in patients less than 16 years of age have not been established.
Geriatric use:
Dose selection for an elderly patient should be judicious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.
Renal impairment:
Dose adjustments are not required for patients with impaired renal function. There are no data in patients with end-stage renal disease undergoing dialysis, and use of Brivaracetam is not recommended in this patient population.
Hepatic impairment:
Because of increases in Brivaracetam exposure, dosage adjustment is recommended for all stages of hepatic impairment.

CONTRAINDICATIONS:
Hypersensitivity: Bronchospasm and Angioedema have been reported in patients taking Brivaracetam. If a patient develops hypersensitivity reactions after treatment with Brivaracetam, the drug should be discontinued. Brivaracetam is contraindicated in patients with a prior hypersensitivity reaction to Brivaracetam or any of the inactive ingredients.

DRUG INTERACTIONS:
- **Rifampin** co-administration with rifampin decreases Brivaracetam plasma concentrations likely because of CYP2C19 induction. Prescribers should increase the Brivaracetam dose by up to 100% (i.e., double the dosage) in patients while receiving concomitant treatment with rifampin.
- **Carbamazepine** co-administration with carbamazepine may increase exposure to carbamazepine-epoxide, the active metabolite of carbamazepine. Though available data did not reveal any safety concerns, if tolerability issues arise when co-administered, carbamazepine dose reduction should be considered.
- **Phenytoin** because Brivaracetam can increase plasma concentrations of phenytoin, phenytoin levels should be monitored in patients when concomitant Brivaracetam is added to or discontinued from ongoing phenytoin therapy.
- **Levetiracetam** Brivaracetam provided no added therapeutic benefit to levetiracetam when the two drugs were co-administered.

INSTRUCTIONS:
- Store below 30°C.
- Protect from heat, sunlight and moisture.
- Keep out of the reach of children.
- To be sold on the prescription of a registered medical practitioner only.

ہدایات:
۳۰ درجہ سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔
گرمی، دھوپ اور نمی سے بچائیں۔
بچوں کی پہنچ سے دور رکھیں۔
صرف مستند ڈاکٹر کے نسخہ پر فروخت کریں۔

PRESENTATION:

Brivatam Tablet 25 mg	:	Pack of 2 x 7 tablets.
Brivatam Tablet 50 mg	:	Pack of 2 x 7 tablets.
Brivatam Tablet 100 mg	:	Pack of 2 x 7 tablets.
Brivatam Oral Solution 10 mg/ml	:	Pack of 60 ml.
Brivatam Injection 50 mg/5ml	:	Pack of 1 ampoule.

FOR FURTHER INFORMATIONS PLEASE CONTACT:

CCL
Manufactured by:
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