BRIVERA

ब्रिभेरा

1. Product Name
BRIVERA 50: Brivaracetam 50 mg Film Coated Tablets IP
BRIVERA 100: Brivaracetam 100 mg Film Coated Tablets IP

2. Name and Strength of Active Ingredient(s)
BRIVERA 50
Each film coated tablets contains:
Brivaracetam IP 50 mg

BRIVERA 100
Each film coated tablets contains:
Brivaracetam IP 100 mg

3. Product Description
BRIVERA is Brivaracetam, an anti-epileptic medication indicated for the treatment of partial-onset seizures in patients with or without secondary generalization. Brivaracetam displays a high and selective affinity for synaptic vesicle protein 2A (SV2A) in the brain, which may contribute to the anticonvulsant effect.

4. Pharmacodynamics & Pharmacokinetics
Pharmacodynamics:
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's anticonvulsant activity.

Pharmacokinetics
Absorption:
Brivaracetam is highly permeable and is rapidly and almost completely absorbed after oral administration. Pharmacokinetics is dose-proportional from 10 to 600 mg (a range that extends beyond the minimum and maximum single-administration dose levels. The median Tmax for tablets taken without food is 1 hour (range 0.25 to 3 hours). Co-administration with a high-fat meal slowed absorption, but the extent of absorption remained unchanged.

Distribution:

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

Metabolism:

Brivaracetam is primarily metabolized by hydrolysis of the amide moiety to form the corresponding carboxylic acid metabolite, and secondarily by hydroxylation on the propyl side chain to form the hydroxy metabolite. The hydroxylation pathway is mediated primarily by CYP2C19. In human subjects possessing genetic variations in CYP2C19, the blood level of brivaracetam itself is increased by 22% or 42%, respectively, in individuals with one or both mutated alleles. CYP2C19 poor metabolizers and patients using inhibitors of CYP2C19 may require dose reduction. An additional hydroxyl acid metabolite is created by hydrolysis of the amide moiety on the hydroxy metabolite or hydroxylation of the propyl side chain on the carboxylic acid metabolite (mainly by CYP2C9). None of the 3 metabolites are pharmacologically active.

Excretion:

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. Fecal excretion accounts for less than 1% of the dose. Less than 10% of the dose is excreted unchanged in the urine. 34% of the dose is excreted as the carboxylic acid metabolite in urine. The terminal plasma half-life (t1/2) is approximately 9 hours.

5. Indications:

Treatment of partial-onset seizures in patients with or without secondary generalization.

6. Recommended Dose and Administration

Monotherapy or Adjunctive Therapy

The recommended dosage for patients is included in table below. In pediatric patients weighing less than 50kg, the recommended dosing regimen is dependent upon body weight. When initiating treatment, gradual dose escalation is not required. Dosage should be adjusted based on clinical response and tolerability.

Recommended Dosage

Age and Body Weight	Initial Dosage	Minimum and Maximum Maintenance Dosage
Adults (16 years and older)	50 mg twice daily (100 mg per day)	25 mg to 100 mg twice daily (50 mg to 200 mg per day)
Pediatric patients weighing 50 kg or more	25 mg to 50 mg twice daily (50 mg to 100 mg per day)	25 mg to 100 mg twice daily (50 mg to 200 mg per day)

7. Contraindications
Hypersensitivity to brivaracetam or any of the inactive ingredients in BRIVERA.

8. Special Populations
Elderly:

In general, 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.

Paediatric population:

Safety and effectiveness of brivaracetam have been established in pediatric patients 1 month to less than 16 years

of age. Use of brivaracetam in these age groups is supported by evidence from adequate and well-controlled studies of brivaracetam in adults with partial-onset seizures, pharmacokinetic data from adult and pediatric patients, and safety data in pediatric patients 2 months to less than 16 years of age.

Pregnancy & Lactation:

Pregnancy Category C. There are no adequate data on the developmental risks associated with use of brivaracetam in pregnant women. In animal studies, brivaracetam produced evidence of developmental toxicity (increased embryofetal mortality and decreased fetal body weights in rabbits; decreased growth, delayed sexual maturation, and long-term neurobehavioral changes in rat offspring) at maternal plasma exposures greater than clinical exposures.

9. Warnings and Precautions

- Suicidal Behavior and Ideation: Monitor patients for suicidal behavior and ideation.
- Neurological Adverse Reactions: Monitor for somnolence and fatigue, and advise patients not to drive or operate machinery until they have gained sufficient experience on brivaracetam.
- Psychiatric Adverse Reactions: Behavioral reactions including psychotic symptoms, irritability, depression, aggressive behavior, and anxiety; monitor patients for symptoms.
- Hypersensitivity: Bronchospasm and Angioedema: Advise patients to seek immediate medical care. Discontinue and do not restart brivaracetam if hypersensitivity occurs.
- Withdrawal of Antiepileptic Drugs: brivaracetam should be gradually withdrawn.

10. Drug-Drug Interactions

- Rifampin: Because of decreased concentrations, increasing brivaracetam dosage in patients on concomitant rifampin is recommended.
- Carbamazepine: Because of increased exposure to carbamazepine metabolite, if tolerability issues arise, consider reducing carbamazepine dosage in patients on concomitant brivaracetam.
- Phenytoin: Because phenytoin concentrations can increase, phenytoin levels should be monitored in patients on concomitant brivaracetam.

11. Undesirable Effects

Adults: Most common adverse reactions are somnolence/sedation, dizziness, fatigue, and nausea/vomiting.

Pediatric Patients: Most common adverse reactions are similar to those seen in adult patients.

12. Storage Condition

Protect from direct sunlight and moisture. Store BRIVERA below 30 ºC at cool and dry place but not in refrigerator. Keep the medication away from children and pets.

13. Dosage Forms and Packaging Available

BRIVERA 50 Tablets:
Each Box contains 15 Tablets X 6 Blisters
BRIVERA 100 Tablets:
Each Box contains 15 Tablets X 6 Blisters

Manufactured by:
Deurali-Janta Pharmaceuticals Pvt. Ltd.
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