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BRIVARACETAM

▼BRIVIACT® FOR EPYLEPSIA (PARTIAL-ONSET SEIZURES)

dtbn
DRUG ASSESSMENT REPORT
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Brivaracetam: one more antiepileptic drug

Indications

Add-on treatment for partial-onset seizures with or without secondary generalization in patients aged > 16 years with epilepsy.

Mechanism of action

As levetiracetam, brivaracetam reduces seizures by attaching to the synaptic vesicle protein 2A (SV2A). When SV2A activity is modulated, the release of neurotransmitters is controlled and neural overactivity is reduced, thereby reducing seizures.

Administration

The starting dose is 50-100 mg/day, depending on patient's response and tolerability. Dose can be either 25 mg twice a day or 50 mg twice a day (morning and evening), with a maximum dose of 150mg/day in patients with liver failure. It is available as film-coated tablets. It must be taken whole with a glass of liquid with or without food. It is also available as an oral solution and as a solution for injection.

Clinical efficacy

No comparisons have been performed. Brivaracetam approval was based on three (n= 1554) double-blind, 12-week, phase III trials where patients were randomized to receive either placebo or brivaracetam at a fixed dose as add-on therapy to regular treatment. Weekly recurrence of partial-onset seizures during treatment was the primary endpoint in two of the trials, whereas it was a secondary endpoint in the third trial (where recurrence was assessed on a 28-day basis). In the latter, the primary endpoint was the rate of response (percentage of patients reporting a reduction of ≥50 in the frequency of seizures), which was a secondary endpoint in the other two trials. The percentage of patients with no seizures was a secondary endpoint in the three trials.

In the three trials, aggregated data analysis yielded statistically significant reductions in the frequency of seizures with respect to placebo (at 28 days) with brivaracetam at all doses (50 mg, 100 mg and 200 mg). The rate of response was significantly higher with all the doses of brivaracetam vs placebo, especially in patients treated with 100mg and 200mg/day, who reached rates of response of 39.5% and 37.8%, respectively.

In a meta-analysis of six RCTs, statistically significant differences were observed in relative risk (1.79; 95%CI: 1.51 to 2.12) and in the rate of patients free from seizures (4.74; 95%CI: 2.00 to 11.25) with brivaracetam. The rate of response was higher in patients on active treatment without levetiracetam as add-on. The EMA has suggested that its efficacy can be inferior in patients previously exposed to levetiracetam.

Brivaracetam, a me-too of levetiracetam

In three open-label long-term trials (30, 90, and 96 months), the rates of drop-out due to lack of efficacy ranged from 11.8 to 39.5%; and the rate of response progressively increased from 43.8 to 72.7% over time.

Safety

Adverse reactions

The most frequent mild to moderate adverse reactions included somnolence (14.3%) and dizziness (11.0%). Somnolence and fatigue (8.2%) became more frequent when the dose increased. The incidence of headache was similar in the group of brivaracetam and placebo.

The rate of drop-outs for adverse reaction was higher in the brivaracetam groups (3.5-4.0%) compared to placebo (1.7%), primarily due to dizziness and convulsions.

Behavioral alterations and severe psychotic disorders were superior with brivaracetam compared to placebo, and their frequency was similar to that observed in levetiracetam. Suicidal ideation was less frequent in patients treated with brivaracetam. The incidence of moderate neutropenia was also higher. No significant differences have been observed in hematologic adverse events between brivaracetam and levetiracetam.

Contraindications

Hypersensitivity to the active ingredient, to other derivatives of pyrrolidone, or any of its excipients.

ABSTRACT

Brivaracetam is an antiepileptic drug used as an add-on treatment, with a similar structure to that of levetiracetam.

No direct comparisons have been performed with brivaracetam and other antiepileptic drugs. A response rate near 40% has been obtained with brivaracetam 100-200 mg/day in pivotal placebo-controlled trials.

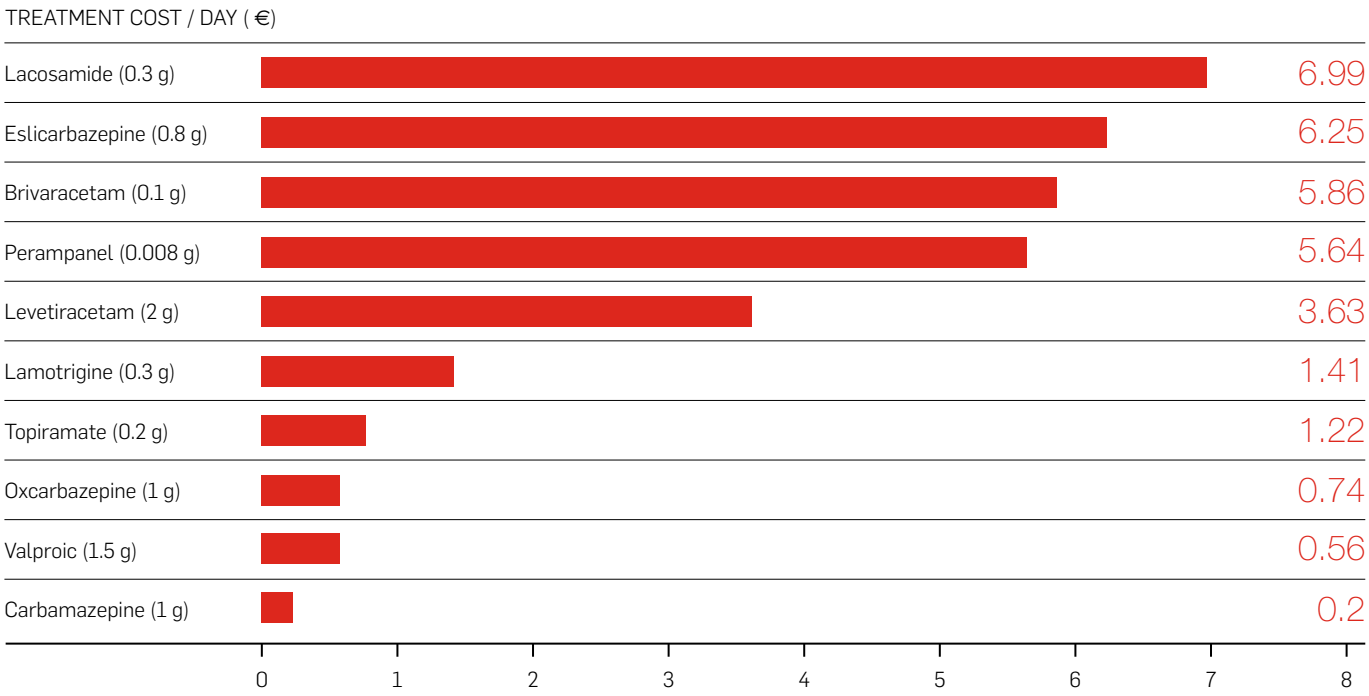
Its safety profile is similar to that of levetiracetam, although the experience is limited. Its most common adverse events include dizziness, somnolence, and fatigue.

Brivaracetam does not make any contribution to therapy as add-on treatment in patients with partial-onset seizures who are unresponsive to other antiepileptic drugs.

CLASSIFICATION

4	IMPORTANT THERAPEUTIC INNOVATION
3	MODEST THERAPEUTIC INNOVATION
2	SOME ADDED VALUE IN SPECIFIC SITUATIONS
1	**NO THERAPEUTIC INNOVATION**
0	INSUFFICIENT EVIDENCE

The qualification assigned to the drug was agreed by the Drug Assessment Committees of Andalusia, Basque Country, Catalonia Institute of Health, Aragon and Navarre. The current report is based on the available information and is susceptible to be updated according to the latest evidence. Let us remind the reader about the importance of notifying the Pharmacovigilance Centre when there are suspicions of adverse reactions to drugs.



Warnings and precautions

The film-coated tablets contain lactose. Patients with hereditary galactose intolerance, Lap lactase insufficiency, or glucose or galactose absorption problems should not take this drug.
It can induce suicidal ideation and attempt.

Use in special situations

Pediatric patients: There are no data on its safety and efficacy in patients aged <16 years. **Renal failure:** Dose adjustment is not required in patients with renal failure. **Liver failure:** The recommended starting dose is 50mg/day. The maximum recommended dose for all patients with liver failure is 150mg twice a day. **Pregnancy and lactation:** No data available.

Interactions

No clinically relevant interactions with other epilepsy drugs have been reported, which is an advantage with respect to traditional epilepsy drugs.
Due to its high lipophilia, it penetrates the blood-brain barrier easily.

Place in therapeutics

Brivaracetam is a new epilepsy drug similar to levetiracetam in terms of structure. It has only been compared with placebo, and no direct comparisons have been undertaken with brivaracetam as add-on treatment to other epilepsy drugs.
Clinical trials have demonstrated that its efficacy is statistically significant –albeit modest–, which is no dose-dependent. It can be less effective in patients previously exposed to levetiracetam, in whom this drug is not recommended. Trials have not demonstrated that the combination of levetiracetam plus brivaracetam is effective, therefore this combination is not recommended. Brivaracetam has a favorable safety profile although the experience is limited. Its cost is 61% higher than that of levetiracetam, without any advantage over the latter.
Given the absence of comparative studies, its moderate efficacy in reducing partial-onset seizures, and its lack of effects on patient's quality of life vs placebo, this medicine does not make any contribution to therapy compared to traditional epilepsy drugs.
Brivaracetam does not provide any therapeutic contribution as add-on treatment in patients with partial-onset seizures who are unresponsive to other epilepsy medicines.

Presentations

Briviact® (UCB PHARMA), 56 tablets, 25 mg; 50 mg; 75 mg; 100 mg (€164.23). Briviact® (UCB PHARMA), oral solution 10 mg/mL, 300 mL (€147.59). Briviact® (UCB PHARMA), solution for injection 10 mg/mL 5 mL, 10 vials (€254.6).

References

Based on the report of contribution to therapy of brivaracetam. Available at https://www.aemps.gob.es/medicamentosUsoHumano/informesPublicos/docs/IPT-brivaracetam-Briviact-epilepsia.pdf

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