

New drugs

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Brivaracetam

Approved indication: epilepsy

Briviact (UCB)

25 mg, 50 mg film-coated tablets, oral solution containing 10 mg/mL

Australian Medicines Handbook section 16.1.3

Temporal lobe epilepsy is the most common of the partial epilepsies. Carbamazepine is generally considered the first-line drug for managing partial epilepsy, but it may not completely control seizures. There are many antiepileptic drugs which can be added such as gabapentin, lamotrigine and levetiracetam. Brivaracetam is another add-on therapy for adults with partial-onset seizures, with or without secondary generalised seizures.

Brivaracetam is thought to act on a protein (SV2A) in the synaptic vesicles. By binding to this protein the drug is thought to alter the release of neurotransmitters into the synapse. The reduction in seizures is proportional to the concentration of brivaracetam in plasma.

It is recommended to begin treatment with 100 mg doses (50 mg twice daily) then adjust the dose according to the response. The tablets are completely absorbed and brivaracetam rapidly enters the brain. Its half-life is about nine hours with most of the dose being metabolised and excreted in the urine. Dose adjustments may be necessary for patients with hepatic impairment and the drug should be avoided in patients with end-stage renal disease on dialysis due to a lack of data. Plasma concentrations of brivaracetam are reduced if it is taken with carbamazepine, phenobarbital (phenobarbitone) or phenytoin.

The approval of brivaracetam is based on the results of three main trials.¹⁻³ The patients in these trials had partial epilepsy that was not controlled by one or two drugs. Different doses of brivaracetam were compared with placebo over 12 weeks.

One trial studied total daily doses of 5 mg, 20 mg or 50 mg in 396 patients. Only the 50 mg dose was significantly better than adding a placebo. This dose reduced weekly seizure frequency by 12.8% more than placebo.¹

A similar trial involving 398 patients studied total daily doses of 20 mg, 50 mg and 100 mg. Respectively, these reduced weekly seizure frequency by 6.8%,


6.5% and 11.7% more than placebo. Only the 100 mg dose made a statistically significant difference.²

The third main trial of brivaracetam involved 768 patients and studied total daily doses of 100 mg and 200 mg. Based on the reduction in seizure frequency during the treatment period, the proportion of patients having a response of 50% or more was significantly higher with brivaracetam. This responder rate was achieved by 38.9% of the patients taking 100 mg, 37.8% of those taking 200 mg and 21.6% of the placebo group. Averaged over a 28-day period, the reduction in seizure frequency was 22.8% greater than placebo for 100 mg and 23.2% greater with 200 mg.³

Across the clinical trials, 6.7% of the patients taking brivaracetam discontinued it because of adverse events. Only 3.9% of the patients given a placebo discontinued. The main reasons for stopping treatment included dizziness, headache and fatigue. Other adverse events caused by brivaracetam include nausea, irritability and somnolence. Some patients become depressed and a few may develop suicidal thoughts. Pooled data suggest the incidence of suicide and suicide attempts is 3.2 per 1000 patient-years.

The clinical trials show that the percentage reduction in seizures is greater than the reduction with placebo. Based on the trial of higher doses, in which patients were having a median of 10 seizures every month, the difference between brivaracetam and placebo is probably two or three seizures per month. Few patients will stop having seizures. In the same trial 5.2% of the patients taking a total daily dose of brivaracetam 100 mg became seizure free.³

An attempt has been made to compare brivaracetam with levetiracetam. This indirect comparison was based on a systematic review of 13 placebo-controlled trials. There were 1919 patients in the brivaracetam trials and 1765 in the levetiracetam trials. For all doses of brivaracetam, there were no statistically significant differences in efficacy.⁴ Some patients who have previously been treated with levetiracetam may respond to brivaracetam, but there is no benefit in using the drugs together.¹⁻³ The systematic review found that levetiracetam was less likely to cause dizziness than higher total daily doses (150 mg, 200 mg) of brivaracetam.⁴

 manufacturer provided additional useful information



Some of the views expressed in the following notes on newly approved products should be regarded as preliminary, as there may be limited published data at the time of publication, and little experience in Australia of their safety or efficacy. However, the Editorial Executive Committee believes that comments made in good faith at an early stage may still be of value. Before new drugs are prescribed, the Committee believes it is important that more detailed information is obtained from the manufacturer's approved product information, a drug information centre or some other appropriate source.

REFERENCES

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The Transparency Score is explained in New drugs: transparency, Vol 37 No 1, Aust Prescr 2014;37:27.

At the time the comment was prepared, information about this drug was available on the websites of the Food and Drug Administration in the USA, the European Medicines Agency and the Therapeutic Goods Administration.