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Brivaracetam: Pharmacology, Clinical Efficacy, and Safety in Epilepsy

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Brivaracetam, a high-affinity synaptic vesicle 2A (SV2A) ligand and propyl analog of levetiracetam, has been approved as an adjunctive and monotherapy option for focal onset seizures in various age groups. This review synthesizes data from both clinical trials and real-world studies to evaluate brivaracetam's efficacy, safety, and tolerability profile. Notably, brivaracetam's rapid penetration across the blood-brain barrier, selective SV2A binding, and favorable pharmacokinetic properties contribute to its robust seizure control capabilities, setting it apart from other antiseizure medications. Studies have shown that brivaracetam consistently achieves significant seizure frequency reductions and high responder rates, demonstrating strong efficacy and an overall favorable safety profile. Importantly, brivaracetam also demonstrates effectiveness in special populations, including older individuals and patients with post-stroke epilepsy, maintaining good tolerability and favorable outcomes and achieving high rates of seizure freedom. Future research should further investigate brivaracetam's utility in broader patient groups to better understand its long-term safety and expand its therapeutic reach. With its unique pharmacological properties, clinical flexibility, and promising safety profile, brivaracetam stands as a valuable addition to current epilepsy treatment options, addressing several unmet needs in seizure management. **(2025;15:42-55)**

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Introduction

Epilepsy is one of the most common neurological disorders, characterized by recurrent seizures that significantly impact patients' quality of life. Despite advances in antiseizure medications, achieving optimal seizure control remains challenging for many patients.

Brivaracetam (BRV), a propyl analog of levetiracetam, functions as an antiseizure medication through its high-affinity binding to synaptic vesicle protein 2A (SV2A).[1] The U.S. Food and Drug Administration first approved BRV in 2016 as an adjunctive treatment for focal onset seizures in patients aged 16 years and older. Subsequently, in 2017, its approval was extended to include monotherapy for focal onset seizures in the same age group. Further expansion of its indications occurred in 2018, allowing its use in patients aged 4 years and older, and in 2021, it was approved for patients aged 1 month and older. In Europe, BRV is currently approved as an adjunctive therapy for focal onset seizures, with or without secondary generalization, in patients aged 2 years and older. In South Korea, the Ministry of Food and Drug Safety approved BRV in 2019 in the form of oral solution and film-coated tablets as adjunctive therapy for focal onset seizures, with or without secondary generalization, in adult and adolescent patients aged 16 years and older with epilepsy. However, despite regulatory approval, BRV has yet to be introduced to the South Korean market.

This review aimed to provide a comprehensive analysis of BRV's pharmacological properties, efficacy, tolerability, and safety profile, synthesizing data from clinical trials and real-world evidence.

Pharmacodynamic properties

BRV belongs to the racetam family and, like levetiracetam (LEV), binds to the SV2A ligand. However, it interacts with a different binding site or conformational state of SV2A.[2] Additionally, BRV exhibits a more selective binding affinity for the SV2A protein, with an affinity 15-30 times higher than that of LEV.[3] SV2A is a transmembrane glycoprotein present in synaptic vesicles in the central nervous system, playing a crucial role in the exocytosis of neurotransmitters from vesicles.[4] BRV inhibits this exocytosis, leading to a reduction in the release of excitatory neurotransmitters.[5] It enters recycling synaptic

vesicles, causing a frequency-dependent decrease in synaptic transmission at concentrations 100 times lower than those required for LEV and more effectively slows synaptic vesicle mobilization.[6]

Initial animal studies suggested that BRV might inhibit voltage-gated sodium channels; however, subsequent studies revealed that BRV does not affect voltage-gated sodium currents in cornu ammonis 1 (CA1) neurons or sustained repetitive firing in cortical and CA1 neurons.[7,8] At therapeutic brain concentrations, BRV did not modulate inhibitory or excitatory postsynaptic ligand-gated ion channels in mouse hippocampal neurons, supporting evidence that its antiepileptic effects stem from its selective action on the presynaptic SV2A protein.[5]

Pharmacokinetic properties

Absorption and distribution

BRV is rapidly absorbed in the intestines following oral administration, exhibiting nearly 100% bioavailability.[9] It demonstrates linear kinetics, with plasma concentrations increasing proportionally to the dose administered.[10] When delivered intravenously, a 100 mg dose of BRV exhibited similar bioavailability to 50 and 100 mg oral tablets.[11] Although the 100 mg intravenous formulation showed a faster rise in plasma levels and a dose-normalized Cmax that was 28% and 21% higher than the 50 and 100 mg oral tablets, respectively, the plasma concentration profiles became similar after the first hour. As a result, the intravenous dose achieved bioequivalence with the oral formulations in terms of overall exposure, as measured by the area under the plasma concentration-time curve from time zero to the last measurable concentration and extrapolated to infinity. These findings suggest that no dose adjustment is necessary when switching between oral and intravenous administration.

Intravenous BRV was well tolerated in a phase III randomized, placebo-controlled trial (NCT01405508) involving 105 epilepsy patients aged 16-70 years with focal or generalized epilepsy uncontrolled by one or two antiseizure medications, with treatment-emergent adverse events (TEAEs) reported in 70.6% of patients initiating intravenous treatment and 66.0% of those transitioning from oral BRV.[12] The incidence of TEAEs was comparable between 2-minute bolus (71.2%) and 15-minute infusion (65.4%) administration methods. Injection-related TEAEs were observed in 9.6% of patients receiving bolus and 11.5% of those receiving infusion. Plasma concentrations were marginally higher in the bolus group following the first dose but became comparable across all groups after the final dose. These findings indicate that intravenous BRV is a viable alternative for patients unable to take oral formulations.

According to a phase 1, randomized, open-label, two-way crossover study involving 24 healthy participants, the pharmacokinetics of BRV were comparable between the 50-mg oral solution and the 50-mg tablet. Both formulations exhibited comparable area under the curve (AUC) values (15.9 and 16.3 μg/hour/mL), confirming bioequivalence. The median Tmax was 0.63 hours for the oral solution and 1.00 hours for the tablet, with similar Cmax values (1.42 vs. 1.34 μg/mL).[9]

BRV is lipophilic and rapidly crosses the blood-brain barrier through passive diffusion, binding to its target site, SV2A.[13] Preclinical studies demonstrated that BRV enters the brain faster than LEV, resulting in a quicker onset of seizure control. This was evidenced by rodent models and supported by positron emission tomography (PET) studies in nonhuman primates.[13] Using the SV2A PET tracer ^{11}C-UCB-J, previous research evaluated brain penetration and occupancy time courses for BRV and LEV at therapeutic doses. In a previous study involving 13 healthy volunteers, BRV demonstrated faster tracer displacement half-time (18 minutes for 100 mg) than LEV (28 minutes for 1,500 mg).[14] It also displayed higher receptor occupancy and a significantly lower half-maximal inhibitory concentration (IC_{50}), suggesting greater potency. IC_{50} reflects the concentration required to inhibit 50% of target activity.

BRV has a half-life of approximately 8-9 hours, a plasma protein binding rate of less than 20%, and a volume of distribution of 0.5-0.6 L/kg.[10] Steady-state concentrations are achieved within 2 days of repeated dosing. While high-fat meals can delay the time to peak plasma concentration (0.5-3.5 hours) and reduce maximum plasma concentration, they do not affect the AUC, ensuring that overall absorption remains consistent.[10]

Metabolism

BRV undergoes extensive metabolism in the liver, primarily via hydrolysis of its acetamide group, producing a carboxylic acid metabolite. This is followed by hydroxylation mediated by cytochrome P450 (CYP) 2C9. A secondary metabolic pathway involves beta-oxidation of the propyl side chain via CYP2C19, resulting in a hydroxy metabolite. A combination of these pathways leads to the formation of a hydroxy-acid metabolite. The three primary metabolites (acid, hydroxy, and hydroxy-acid) are pharmacologically inactive.[15] Although the levels of these metabolites increase in patients with reduced renal clearance, this does not result in significant adverse effects, and dose adjustment is

typically not required.[16] However, this conclusion is based on studies that excluded patients undergoing dialysis; therefore, caution is advised in this population. Conversely, BRV exposure increases by 50-60% in patients with hepatic impairment due to altered biotransformation, including reduced CYP-dependent hydroxylation and increased CYP-independent acid metabolite formation. Consequently, a dose reduction is recommended in patients with hepatic impairment.[17]

Elimination

BRV is primarily excreted through the kidneys, with over 90% of the administered dose eliminated within 2 days. Of this, 8.6% is excreted in the urine as unmetabolized BRV.[18]

Pharmacokinetic drug interactions

BRV has a low potential to affect the activity of cytochrome P450 enzymes.[18] A study analyzing five randomized, double-blind, placebo-controlled efficacy trials reported that BRV does not influence the steady-state plasma concentrations of commonly prescribed antiseizure medications, including levetiracetam, lacosamide, lamotrigine, phenobarbital, pregabalin, phenytoin, topiramate, valproate, and zonisamide.[19]

In a phase I open-label study, BRV co-administration with carbamazepine did not significantly alter carbamazepine AUC over a dosing interval but increased levels of carbamazepine-epoxide, an active metabolite.[20] BRV inhibited the *in vitro* hydrolysis of carbamazepine-epoxide in human hepatocytes, demonstrating an IC_{50} value of 8.2 μM. Carbamazepine modestly decreased BRV AUC while increasing its oxidative metabolism. A *post-hoc* analysis of pooled data from phase III studies indicated that the increase in carbamazepine-epoxide levels did not lead to clinically significant adverse events, suggesting that dose adjustments are not necessary when BRV and carbamazepine are co-administered.[21]

In addition to interactions mediated by metabolic enzymes, the potential influence of BRV on drug transporters has also been investigated. *In vitro* studies suggest that BRV does not meaningfully inhibit or induce key transporters, including P-glycoprotein (P-gp).[22] As a result, it is unlikely that BRV would alter the P-gp-mediated efflux of common substrates such as digoxin or newer oral anticoagulants, including apixaban, dabigatran, edoxaban, and rivaroxaban.[23] Collectively, these findings support the notion that BRV carries a low risk of clinically relevant drug transporter-mediated drug interactions.

Doses of BRV at 400 mg/day, when taken with oral contraceptives (OCs) in healthy women (n=24), led to a 27% reduction in plasma levels of ethinyl estradiol and a 23% reduction in levonorgestrel levels.[24] However, endogenous hormone levels remained unchanged, and ovulation did not occur in any participant. At the therapeutic dose of BRV 100 mg/day, no interaction was observed when co-administered with OCs; there were no changes in plasma concentrations of ethinyl estradiol or levonorgestrel, and OCs did not affect BRV trough levels.[25]

A study investigating the impact of rifampin, a potent inducer of CYP3A4, -2B6, -2C8, -2C9, and -2C19 enzymes, on BRV pharmacokinetics found that BRV's AUC was reduced by 45% when co-administered with rifampin.[26] This suggests that an increased dose of BRV may be necessary for patients taking rifampin concurrently.

A double-blind, randomized study in healthy males showed that co-administration of BRV and ethanol did not result in significant pharmacokinetic interactions. However, ethanol significantly increased its effects on psychomotor function, attention, and memory, including reduced alertness, impaired coordination, and decreased word recall.[27]

Therapeutic efficacy

Adjunctive therapy in focal onset seizure

The first study to evaluate the therapeutic potential of BRV was the phase IIA study (NCT00401648), which assessed single doses of BRV at 10, 20, 40, and 80 mg in 18 patients with photosensitive epilepsy using a subject-blind, placebo-controlled design.[28] Results showed that BRV completely suppressed generalized photosensitive responses in 78% of participants. BRV was well tolerated, with no reports of serious adverse events. The most common TEAEs were dizziness and somnolence.

Two exploratory, double-blind, randomized, placebo-controlled phase IIB dose-ranging studies were conducted to evaluate BRV in patients with refractory focal onset seizures, despite treatment with one or two antiseizure medications. In the study (NCT00175825), by French et al.,[29] 208 patients underwent a 7-week treatment period without up-titration, comparing placebo with BRV at doses of 5, 20, and 50 mg as adjunctive therapy. The primary efficacy endpoint was the percent reduction in focal seizure frequency per week relative to placebo. Estimated reductions in seizure frequency per week were 9.8% for 5 mg (p=0.240), 14.9% for 20 mg (p=0.062), and 22.1% for 50 mg (p=0.004), with statistical significance achieved at the 50

mg dose. Median reductions in focal seizure frequency per week from baseline were 21.7% for placebo, 29.9% for BRV 5 mg (p=0.086), 42.6% for BRV 20 mg (p=0.014), and 53.1% for BRV 50 mg (p<0.001), with the 20 and 50 mg doses showing statistical significance. BRV was well tolerated, with most adverse events being mild to moderate. Only 2.6% of participants discontinued due to adverse events. In contrast, the study (NCT00175929) by Van Paesschen et al.[30] involving 157 patients in the intent-to-treat population did not demonstrate a statistically significant effect for BRV at 50 mg or 150 mg. Following a 3-week up-titration period, the study compared BRV 50 and 150 mg with placebo over a 7-week maintenance period. The primary efficacy outcome, the percent reduction in seizure frequency per week compared to placebo during the maintenance period, was 14.7% for the 50 mg/day group (p=0.093) and 13.6% for the 150 mg/day group (p=0.124), neither of which achieved statistical significance. However, during the entire treatment period, reductions in focal seizure frequency per week were observed: 17.7% in the 50 mg/day group (p=0.026) and 16.3% in the 150 mg/day group (p=0.043). TEAEs were mostly mild, with similar rates across groups: 67.9% in the BRV 50 mg group, 67.3% in the BRV 150 mg group, and 71.2% in the placebo group.

In a prospective, double-blind, fixed-dose phase III study (NCT00464269) conducted by Biton et al.,[31] 400 patients with at least eight focal seizures during an 8-week baseline period were randomized in a 1:1:1:1 ratio to receive placebo or BRV at doses of 5, 20, or 50 mg twice daily. The primary efficacy endpoint, the percent reduction in seizure frequency per week compared to placebo, was -0.9% (p=0.885) for BRV 5 mg/day, 4.1% (p=0.492) for BRV 20 mg/day, and 12.8% (p=0.025) for BRV 50 mg/day. The study concluded that only the 50 mg/day dose demonstrated statistically significant reductions in seizure frequency.

In a phase III study (NCT00490035) conducted by Ryvlin et al.,[32] 399 patients were randomized to receive a placebo, 20, 50, or 100 mg of BRV per day for 12 weeks without up-titration. The percent reduction in seizure frequency compared to placebo was 6.8% (p=0.239) for BRV 20 mg/day, 6.5% (p=0.261) for BRV 50 mg/day, and 11.7% (p=0.037) for BRV 100 mg/day. Unlike the study by Biton et al.,[31] the 50 mg/day dose in this trial did not achieve statistical significance, but the 100 mg/day dose showed efficacy.

The phase III study (NCT01261325) by Klein et al.[33] aimed to confirm the efficacy, safety, and tolerability of BRV in adults. This randomized, double-blind, multicenter study excluded patients who had taken LEV within 90 days prior to the trial. After an 8-week prospective baseline period, 768 patients were randomized in a 1:1:1 ratio to receive a placebo, BRV 100 mg/day, or BRV 200 mg/day for a 12-week treatment period. Percent reductions in seizure frequency over 28 days compared to placebo were 22.8% for BRV 100 mg/day (p<0.001) and 23.2% for BRV 200 mg/day (p<0.001), confirming the efficacy of both doses for adjunctive treatment without concomitant LEV. TEAEs occurred in 59.4% of placebo patients and 67.6% of BRV-treated patients, with discontinuation rates due to TEAEs at 3.8% for placebo, 8.3% for BRV 100 mg/day, and 6.8% for BRV 200 mg/day. The most common TEAEs in the BRV group were somnolence (18.1% vs. 7.7% in placebo), dizziness (12.3% vs. 5.0%), and fatigue (9.5% vs. 3.8%).

A pooled clinical analysis was conducted using patient data from three pivotal studies (NCT00464269, NCT00490035, and NCT01261325), focusing on adult patients with focal onset seizures not controlled with one to two antiseizure medications.[34] Patients were randomized to receive BRV dosages of 50, 100, or 200 mg/day, or a placebo, without up-titration, with concomitant LEV use excluded in studies NCT00464269 and NCT00490035. The percent reduction in focal onset seizure frequency over 28 days compared to placebo was 19.5% for 50 mg/day (p=0.001), 24.4% for 100 mg/day (p<0.001), and 24.0% for 200 mg/day (p<0.001). The ≥50% responder rates were significantly higher for BRV at 34.2% (50 mg/day), 39.5% (100 mg/day), and 37.8% (200 mg/day) compared to 20.3% for placebo, with 90.0% to 93.9% of participants completing the studies. TEAEs were reported in 68.0% of BRV patients and 62.1% of placebo patients, with serious TEAEs occurring in 3.0% and 2.8%, respectively. The most common TEAEs with BRV were somnolence (15.2%), dizziness (11.2%), and fatigue (8.7%).

In the data pooled from three phase III studies (NCT00490035; NCT00464269; and NCT01261325), involving 409 patients with secondarily generalized tonic-clonic seizures (SGTCS) during baseline, adjunctive BRV at doses of 50-200 mg/day without titration over a 12-week treatment period significantly reduced the frequency of SGTCS over 28 days, with median reductions of 66.6%, 61.2%, and 82.1% for BRV 50, 100, and 200 mg/day, respectively, compared to 33.3% for placebo.[35] The ≥50% responder rates were 61.3%, 55.0%, and 64.0% for BRV doses compared to 33.0% for placebo, all of which were statistically significant. During the 12-week treatment period, 30.4% of patients who were administered BRV at doses of 50 mg/day or higher became completely free of SGTCS. BRV was well tolerated, with TEAEs reported in 65.0% of BRV patients receiving ≥50 mg/day vs. 60.6% for placebo.

Kwan et al.[36] conducted a phase III, placebo-controlled trial

(NCT00504881) in adults to evaluate the safety and tolerability of flexible doses (20-150 mg/day) of adjunctive BRV in patients whose epilepsy remained uncontrolled despite treatment with 1-3 antiseizure medications. For patients with focal seizures, the median percent reduction in baseline-adjusted seizure frequency per week was 26.9% for BRV compared to 18.9% for placebo (p=0.070), with a ≥50 responder rate of 30.3% vs. 16.7% for placebo (p=0.006). Notably, this study included patients with generalized epilepsy (49 patients total; 36 in the BRV group and 13 in the placebo group). Among patients with generalized seizures, BRV reduced seizure days per week by 42.6% compared to 20.7% for placebo, with ≥50% responder rates of 44.4% for BRV and 15.4% for placebo. Adverse events occurred at similar rates in both the BRV (66.0%) and placebo (65.3%) groups.

Adjunctive therapy in generalized epilepsy and Unverricht-Lundborg disease

BRV has shown more complete suppression of spontaneous spike-and-wave discharges in genetic absence epilepsy rats compared to LEV, demonstrating greater potency and efficacy in experimental models of epilepsy.[37] Additionally, previous phase IIA study has shown that BRV effectively suppresses generalized photoparoxysmal electroencephalographic responses.[28]

In a retrospective cohort study of 37 adults with genetic generalized epilepsy (mean age, 29.9±12.3 years; 73% female), the 6-month retention rate of BRV was 81.1%, with 83.8% achieving a ≥50% seizure reduction and 62.2% achieving seizure freedom.[38] BRV was initiated primarily due to lack of efficacy (51.4%) or adverse events (27.0%) from prior antiseizure medications, and 32.4% of patients received BRV as monotherapy. A higher number of prior antiseizure medication exposures was associated with a lower response rate (p<0.05). Resolution of LEV-related adverse events was observed in 79.8% of affected patients.

A multicenter, retrospective cohort study evaluated the effectiveness, retention, and tolerability of BRV in 61 patients with genetic generalized epilepsies who initiated treatment in 2016-2017 (mean age, 29.8 years; range, 9-90 years; 67% female).[39] The study population consisted of patients with difficult-to-control epilepsy, having failed an average of 2.4 antiseizure medications in the past and taking 1.9 antiseizure medications at baseline. Retention rates for BRV were 82% at 3 months and 69% at 6 months, with a 50% responder rate of 36% at 3 months and 28% for over 6 months. Among patients with juvenile myoclonic epilepsy, 60% were responders at 3 months, and 40% achieved seizure freedom. BRV was well-tolerated, with treatment-emergent adverse events reported in 26% of patients, including somnolence, ataxia, and psychobehavioral symptoms.

Kälviäinen et al.[40] conducted two phase III trials to evaluate the efficacy, tolerability, and safety of adjunctive BRV in patients with Unverricht-Lundborg disease. Results indicated that BRV did not achieve a statistically significant reduction in action myoclonus scores compared to placebo, with considerable variability in patient scores. However, both trials had high completion rates (95.3%), and most participants (88.7%) continued into long-term follow-up, likely owing to BRV's favorable tolerability.

According to Lince-Rivera et al.,[41] a narrative review identified 360 records about BRV and genetic generalized epilepsy through a systematic search, with 32 studies ultimately included after exclusions. BRV, administered at doses of 50-200 mg/day, showed >50% responder rates ranging from 36% to 84%, with drug-associated adverse events reported in 24-57% of cases. Most studies demonstrated favorable tolerability, high retention rates, and an absence of serious adverse effects, even in refractory cases, special populations, and patients with prior LEV failure.

These findings support BRV as an effective and well-tolerated treatment option for genetic generalized epilepsies (Table 1).

Long-term efficacy

A *post hoc* analysis by Moseley et al.[42] evaluated the long-term efficacy, tolerability, and health-related quality of life associated with adjunctive BRV in adults with focal to bilateral tonic-clonic seizures. The study included 284 patients from randomized, placebo-controlled trials who received BRV at doses of 50-200 mg/day.[42] Over a median treatment duration of 2.5 years, BRV reduced the frequency of focal to bilateral tonic-clonic seizures by 76.2%, with 68.7% of patients achieving a 50% reduction and 50.7% achieving a 75.0% reduction. Quality of life improvements were reported by 43.6% of patients after 1 year and 46.4% after 2 years. Kaplan-Meier analysis indicated that long-term adjunctive BRV was well tolerated, with retention rates of 69.3% at 1 year, 48.2% at 3 years, and 37.3% at 5 years.

A pooled analysis by Toledo et al.[43] reported long-term seizure outcome data from phase IIb, III/IIIb, and long-term follow-up studies assessing the safety, tolerability, and efficacy of BRV in adults with focal seizures. Among 2,186 patients treated with BRV 50-200 mg/day, retention rates were 91.0% at 6 months and 54.4% at 60 months, with a total BRV exposure of 5,339.4 patient-years (≥8.0 years in 41 patients). TEAEs were reported by 84.5% of patients,

Table 1. Efficacy of adjunctive BRV in patients with epilepsy

Study (study design)	BRV dose (mg/d)	No. of patients	≥50% responder rate (%)		Seizure free rate (%)	
			Focal	Generalized	Focal	Generalized
Ben-Menachem et al.[34] (three pooled clinical studies)	PL	459	20.3		0.5	
	50	200	34.2*		2.5	
	100	353	39.5‡		5.1†	
	200	250	37.8‡		4.0‡	
Kwan et al.[36] (phase III RCT)	PL	108	16.7		0.0	
	Flex dose (20-150)	323	30.3†		1.5	
	PL	13		15.4		0.0
	Flex dose (20-150)	36		44.4		5.6
Strzelczyk et al.[39] (retrospective cohort)	Flex dose (25-200)	56		36.0		25.0
Inoue et al.[45] (phase III RCT)	PL	149	19.0		0.0	
	50	151	41.1†		4.6*	
	100	148	49.3†		6.8†	

BRV, brivaracetam; PL, placebo; RCT, randomized controlled trial.
*$p<0.05$.
†$p<0.01$.
‡$p\leq0.001$.

with the most common being headache, dizziness, and somnolence. BRV reduced the frequency of focal onset seizures by a median of 48.8%, with a ≥50% responder rate of 48.7%. Complete seizure freedom rates were 4.9%, 4.2%, 3.0%, and 3.3% for ≥6, 12, 24, and 60 months, respectively, demonstrating sustained seizure control over time. Improvements in health-related quality of life, as measured by the quality of life in epilepsy inventory-31, were also observed.

An open-label, multinational follow-up trial (NCT00150800) led by O'Brien et al.[44] evaluated the long-term safety, tolerability, and efficacy of adjunctive BRV at individualized doses up to 200 mg/day in patients aged 16 years and older with epilepsy who had completed prior double-blind, placebo-controlled trials of adjunctive BRV (NCT00175825, NCT00490035, NCT00464269, or NCT00504881). The study included 667 patients, of whom 97.8% had focal seizures, with 49.2% exposed to BRV for 48 months or more. TEAEs occurred in 91.2% of patients, leading to discontinuation in 14.8% of cases. The most common TEAEs were headache (25.3%) and dizziness (21.9%), while psychiatric TEAEs, including depression (10.6%), insomnia (7.3%), and anxiety (6.7%), were reported by 31.8% of patients. Psychiatric TEAEs led to discontinuation in 5.1% of patients, with suicidal ideation accounting for 1.2%. The median reduction in focal seizure frequency per 28 days was 57.3% at 12 months, increasing to 67.1% at 36 months and stabilizing at 74.3% through 108 months. The overall 50% responder rate was 55.6%, showing an improvement trend by exposure duration cohort. During the trial, 170 patients (30.3%) achieved seizure freedom for at least 6 months, and 114 patients (20.3%) achieved seizure freedom for at least 12 months. In the 132-month cohort, four patients were seizure-free for 6 years, 3 for 8 years, and 1 for 10 years. Quality of life scores showed modest improvements, with efficacy outcomes improving with longer exposure and stabilizing after 9 years. Overall, BRV was well tolerated, providing sustained seizure control over the long term.

Adjunctive therapy in Asia

Inoue et al.[45] recently published a phase III, randomized, double-blind, placebo-controlled study evaluating the efficacy, safety, and tolerability of adjunctive BRV in 449 adult Asian patients with focal-onset seizures. Patients were randomized to receive a placebo, BRV 50 mg/day, or BRV 200 mg/day over a 12-week treatment period. BRV significantly reduced focal-onset seizure frequency, with a 24.5% reduction for the 50 mg/day group and a 33.4% reduction for the 200 mg/day group compared to placebo. The 50% responder rate was 41.1% for BRV 50 mg/day and 49.3% for BRV 200 mg/day, compared to 19.0% for placebo. Seizure freedom was achieved by 4.6% of patients on BRV 50 mg/day and 6.8% on BRV 200 mg/day, while no patients on placebo achieved seizure freedom. TEAEs were reported in 58.5% of patients on BRV, similar to 58.4% in the placebo group. Serious TEAEs occurred in 2.0% of BRV patients compared to 0.7% on placebo, and TEAEs leading to discontinuation occurred

in 3.0% of BRV patients compared to 4.7% on placebo. Overall, BRV was found to be both efficacious and well tolerated, with safety and efficacy profiles consistent with those seen in non-Asian populations.

Monotherapy

BRV was recently approved in the USA as monotherapy for patients aged 16 years or older with focal seizures.

Two phase III conversion-to-monotherapy studies (NCT00698581 and NCT00699283) evaluated its efficacy in adults aged 16-75 years, using a primary endpoint of cumulative exit rate over 112 days compared to a historical control threshold of 0.722.[46] Exit criteria included significant increases in seizure frequency, new seizure types, or status epilepticus during the tapering of baseline antiseizure medications. In the 50 mg/day group, cumulative exit rates were 0.487 (95% confidence interval [CI], 0.347-0.626) and 0.474 (95% CI, 0.310-0.638) in the respective studies, both below the historical control threshold. However, with sensitivity analyses cumulative exit rates were above historical control. Therefore, results should be interpreted with caution as, following termination of both studies, patient numbers were too low to evaluate the effiacy of BRV monotherapy.

The BRIVA-ONE study evaluated the 12-month efficacy and safety of BRV monotherapy either as first-line or conversion to monotherapy in 276 patients aged ≥18 years with epilepsy.[47] The results showed a retention rate of 89.9% (87.5% for first-line monotherapy group; 90.4% for conversion-to-monotherapy group) and a seizure freedom rate of 77.8% (75.0% for first-line monotherapy group; 78.4% for conversion-to-monotherapy group) at 12 months. Adverse events were reported in 39.5% of patients, most of which were mild to moderate. BRV also demonstrated similar efficacy as a first-line and as a conversion-to-monotherapy treatment, with consistent effectiveness and safety in older patients and those with various epilepsy etiologies.

A phase 2/3, randomized, double-blind, placebo-controlled trial (NCT04666610) is currently recruiting participants to evaluate the efficacy, safety, and tolerability of BRV as monotherapy in patients aged 2-25 years with childhood absence epilepsy or juvenile absence epilepsy.[48] This study features a two-stage adaptive design, including a screening period, placebo-controlled and active treatment periods, followed by a randomized withdrawal phase for patients achieving seizure freedom. This trial is important in advancing treatment for generalized epilepsy, particularly in younger patients.

According to a study using data from three phase III add-on trials and two terminated phase III monotherapy trials, BRV was evaluated as monotherapy for focal seizures in adults by extending a population pharmacokinetic model to include the effects of 12 commonly prescribed antiseizure medications.[49] Simulations showed that BRV's dose-response relationship in monotherapy aligns with that in adjunctive therapy, with a 22.6% increase in plasma concentration observed in the absence of enzyme-inducing antiseizure medications. The study concluded that BRV maintains efficacy at doses of 50-200 mg/day, supporting its use as monotherapy without the need for dose adjustments.

In conclusion, BRV shows significant potential as a monotherapy option for focal seizures. Its favorable safety profile and predictable pharmacokinetics make it a valuable treatment alternative.

Real-world evidence on the effectiveness and tolerability of BRV

In a multicenter retrospective study (BRIVA-LIFE) of 575 patients with focal epilepsy, BRV treatment over 12 months resulted in a mean seizure frequency reduction of 36.0%, with 39.7% of patients achieving a ≥50% seizure reduction and 17.5% attaining seizure freedom.[50] Notably, seizure freedom was observed in 37.5% of patients aged 65 years or older. Adverse events were reported in 39.8% of patients, psychiatric adverse events in 14.3%, and treatment discontinuation due to adverse events occurred in 8.9% overall and 3.7% for psychiatric adverse events.

A pooled analysis of adult patients initiating BRV in clinical practice further demonstrated its broad applicability across various comorbidities and epilepsy etiologies.[51] At 12 months, ≥50% seizure reduction rates were 35.6% in patients with cognitive or learning disabilities, 38.7% in those with psychiatric comorbidities, 41.7% in patients with post-stroke epilepsy, 34.1% in those with brain tumor-related epilepsy, and 50.0% in those with traumatic brain injury-related epilepsy. Continuous seizure freedom rates ranged from 5.7% to 29.4% across these groups. BRV discontinuation rates varied between 27.1% and 39.7%, while TEAEs were reported in 3.0% to 16.7% of patients.

Collectively, these real-world findings consistently support the effectiveness and favorable tolerability profile of BRV across diverse comorbidities and epilepsy etiologies.

Safety and tolerability

General profiles

BRV has shown a robust safety profile in clinical trials and real-world studies. Key findings from pivotal studies and pooled analyses highlight its favorable tolerability and effectiveness.

Real-world evidence from the BRIVA-LIFE study provides additional support for BRV's safety.[50] TEAEs were reported in 39.8% of patients, with somnolence (14.1%), irritability (10.4%), and dizziness (9.2%) being the most common. Psychiatric adverse events, observed in 14.3% of patients, were notably lower than those associated with LEV, reflecting BRV's reduced likelihood of causing behavioral side effects. Discontinuation due to TEAEs occurred in only 8.9% of patients, reinforcing its strong tolerability in clinical practice. A *post-hoc* analysis of 1,160 patients examined BRV's safety in those previously exposed to antiseizure medications, including LEV.[52] The findings showed that the TEAE rate was comparable between antiseizure medication-exposed and antiseizure medication-naïve patients, with discontinuation rates due to TEAEs remaining under 5% across all BRV dose groups (50-200 mg/day).

A *post hoc* analysis of pooled data from three double-blind, placebo-controlled trials (NCT00490035, NCT00464269, and NCT01261325) evaluated BRV (50-200 mg/day) in patients with focal-onset seizures using nine common concomitant antiseizure medications: carbamazepine, lamotrigine, valproate, oxcarbazepine, topiramate, phenytoin, lacosamide, clobazam, and phenobarbital.[53] The overall incidence of TEAEs was similar across subgroups by specific concomitant antiseizure medications with 60.8-74.5% of BRV-treated patients and 53.8-66.7% on placebo reporting TEAEs. Drug-related TEAEs occurred in 35.2-48.3% of BRV patients compared to 23.9-37.1% of placebo patients. Discontinuation due to TEAEs ranged from 2.9% to 13.3% for BRV and 0% to 5.7% for placebo.

An analysis of pooled data from two phase II and four phase III placebo-controlled trials involving a total of 1,957 patients (1,271 on adjunctive BRV and 686 on placebo) was conducted to assess BRV's safety profile for treating focal seizures.[54] The incidence of TEAEs was 66.9% with BRV and 62.8% with placebo. Common TEAEs associated with BRV included somnolence (13.3%), headache (10.5%), dizziness (10.0%), and fatigue (8.2%). Across the therapeutic dose range of BRV, no clear patterns or dose-dependent trends were observed in the occurrence of TEAEs. Psychiatric disorder-related TEAEs occurred in 11.3% of BRV-treated patients compared to 8.2% in the placebo, while behavioral disorder-related TEAEs were low (4.0% BRV vs. 2.5% placebo). While BRV's psychiatric adverse events were higher than placebo, their overall incidence remains relatively low.

Previous study also evaluated the safety profile of BRV when administered intravenously, pooling data from two clinical pharmacology trials; N01256 (UCB Pharma, Brussels, Belgium, data on file) and NCT01796899, and one phase III trial, NCT01405508.[11,12] Based on pooled safety data from these studies, which included 104 patients with epilepsy and 49 healthy individuals who received intravenous BRV in doses ranging from 25 mg to 150 mg, TEAEs reported in ≥3% of participants were generally mild to moderate in intensity. The most frequently observed TEAEs included somnolence (30.1%), dizziness (15.7%), fatigue (15.0%), headache (7.2%), dysgeusia (6.5%), euphoric mood (3.9%), feeling drunk (3.9%), and infusion site pain (3.3%). These findings support intravenous BRV as a well-tolerated alternative when oral administration is not feasible (Table 2).

Table 2. Treatment-emergent adverse events classified as nervous system disorders reported in ≥1% of all patients receiving brivaracetam (BRV)[51]

	Placebo (n=686)	BRV randomized daily dose				BRV overall (n=1,271)
		50 mg (n=360)	100 mg (n=440)	150 mg (n=221)	200 mg (n=250)	
Somnolence	54 (7.9)	41 (11.4)	70 (15.9)	16 (7.2)	42 (16.8)	169 (13.3)
Headache	79 (11.5)	52 (14.4)	40 (9.1)	22 (10.0)	19 (7.6)	133 (10.5)
Dizziness	48 (7.0)	35 (9.7)	43 (9.8)	13 (5.9)	36 (14.4)	127 (10.0)
Irritability	10 (1.5)	14 (3.9)	11 (2.5)	2 (0.9)	7 (2.8)	34 (2.7)
Convulsion	18 (2.6)	9 (2.5)	13 (3.0)	6 (2.7)	3 (1.2)	31 (2.4)
Tremor	10 (1.5)	4 (1.1)	6 (1.4)	4 (1.8)	4 (1.6)	18 (1.4)
Memory impairment	9 (1.3)	5 (1.4)	4 (0.9)	2 (0.9)	3 (1.2)	14 (1.1)

Values are presented as number (%).

Special populations

Older adults

Safety, tolerability, and efficacy data for patients aged ≥65 years were pooled from three randomized, double-blind, placebo-controlled, fixed-dose phase III studies (NCT00490035, NCT00464269, and NCT01261325).[55] A total of 32 older patients were randomized to receive either a placebo or BRV at doses of 50, 100, or 200 mg/day, with 93.8% completing the study. TEAEs occurred in 87.5% of placebo-treated and 73.3% of BRV-treated patients, with no drug-related serious adverse events or deaths reported during the treatment period. Median seizure reduction rates were 14.0% for placebo and up to 74.9% for BRV at 200 mg/day, suggesting BRV's efficacy and tolerability in older patients with focal seizures.

A recent subgroup analysis from the international EXPERIENCE study demonstrated greater effectiveness in older patients (aged ≥65 years) compared to younger adults (aged ≥16 years to <65 years) with epilepsy.[56] At 12 months, a higher percentage of older patients achieved ≥50% seizure reduction (46.5% vs. 36.0%), seizure freedom (26.0% vs. 13.9%), and continuous seizure freedom (22.0% vs. 10.7%) compared to the younger subgroup, indicating that BRV may be particularly effective in older adults.

The BRIVAFIRST study evaluated 1,029 patients with focal epilepsy, including 111 aged ≥65 years.[57] At 12 months, seizure freedom was achieved in 31.5% of older patients vs. 14.6% of younger patients (p<0.001). Adverse events occurred in 24.2% of older patients, and treatment discontinuation was lower in older (18.0%) than younger patients (26.7%; p=0.048). Adjunctive BRV showed good effectiveness and tolerability in older adults. A study by Stockis et al.[58] evaluated the pharmacokinetics, metabolism, safety, and tolerability of BRV in 16 healthy older participants aged 65 years to 78 years. Participants received a single 200-mg dose on day 1, followed by 200 mg twice daily for 10 days. Regular monitoring of adverse events, vital signs, electrocardiograms, laboratory tests, neurological assessments, and psychometric scales detected no clinically significant changes or abnormalities. Adverse events were mostly mild and consistent with previous trials, and pharmacokinetics were similar to those observed in younger populations, suggesting that dose adjustments are not necessary for older adults.

These findings suggest that BRV may offer a well-tolerated and effective treatment option for older patients, who often face challenges with polypharmacy and comorbidities. Further studies are warranted to explore its long-term safety and real-world applications in this population.

Pediatrics

In a phase IIa, open-label, single-arm, three-step fixed dose escalation trial (NCT00422422) over 3 weeks, 99 children aged 1 month to <16 years with epilepsy received BRV oral solution alongside 1-3 concomitant antiseizure medications.[59] Doses were increased weekly (0.8, 1.6, 3.2 mg/kg/day for ≥8 years; 1.0, 2.0, 4.0 mg/kg/day for <8 years). TEAEs occurred in 66.7% and drug-related TEAEs in 32.3%, most commonly somnolence (7.1%) and decreased appetite (6.1%), while ≥50% responder rates were 21.3% overall and 36.4% in focal seizure patients aged 4 years to <16 years.

Following this initial trial, an interim analysis pooled data from two open-label, single-arm, multicenter trials: NCT00422422 (a 3-week trial of BRV 0.8-4.0 mg/kg/day in patients aged 1 month to <16 years) and NCT01364597 (a long-term follow-up with BRV 1-5 mg/kg/day, maximum 200 mg/day, directly enrolling patients aged 4 years to <17 years with focal seizures).[60] Among 149 patients analyzed, 90 were still receiving BRV at the cut-off, with a total exposure of 299.4 patient-years. TEAEs occurred in 94.0% and drug-related TEAEs in 37.6%, most commonly somnolence (6.0%), with two deaths unrelated to BRV. Overall, adjunctive BRV was generally well tolerated in children aged 4 years to <16 years with focal seizures.

In another study of 93 children (mean age, 11.5±7.5 years) with a wide spectrum of pediatric epilepsy, including epileptic encephalopathy and generalized epilepsy, the BRV retention rate was 80.6% at 3 months, 66.7% at 6 months, and 45.2% at 12 months.[61] The overall responder rate was 25.8% at 3 months and around 17.0% at 6 months and 12 months, with no responders among patients with epileptic encephalopathy. About 75.3% of patients reported no adverse events, indicating favorable tolerability. In this study, BRV was introduced through an overnight switch from LEV in 29 patients (30.1%), with five patients (17.2%) experiencing a reduction in behavioral adverse effects.

Long-term safety and efficacy were further assessed in a phase 3, open-label, multicenter long-term follow-up trial (NCT01364597), which evaluated BRV in 257 pediatric patients (aged 1 month to <17 years) with epilepsy, focusing on TEAEs, behavior, and seizure outcomes.[62] Among these patients, 93.4% experienced TEAEs, 32.3% had serious TEAEs, and seven deaths occurred (none treatment-related). Median 28-day focal seizure frequency decreased by 62.9% in patients ≥2 years and 96.9% in those <2 years, with ≥50% responder rates of 50.9 and 68.2%, respectively. Cognitive

and behavioral profiles remained generally stable over time.

Finally, a meta-analysis of nine studies including 503 children with epilepsy reported a BRV retention rate of 78%, a ≥50% responder rate of 35%, and a seizure freedom rate of 18%.[63] The incidence of TEAEs was 39.0%, with somnolence (9.0%) and mental or behavioral disorders (12.0%) being the most common adverse events, further supporting the favorable safety and efficacy profile of BRV in childhood epilepsy.

In conclusion, BRV demonstrated consistent efficacy, good long-term tolerability, and stable cognitive/behavioral outcomes across multiple pediatric studies, supporting its role as a valuable treatment option for children with epilepsy. However, while the existing evidence offers meaningful guidance for BRV treatment in childhood epilepsy, direct clinical studies and comprehensive meta-analyses are still lacking.

Post-stroke epilepsy

A subgroup analysis including 51 patients with and 1,397 patients without post-stroke epilepsy from the international EXPERIENCE pooled data compared BRV retention rates, efficacy, and tolerability.[51] The retention rates at 12 months were similar, with 70.0% for patients with post-stroke epilepsy and 71.3% for patients with non-post-stroke epilepsy. At 12 months, 41.7% of patients with post-stroke epilepsy and 36.7% of those without achieved a ≥50% reduction in seizures. Seizure freedom was more common in the post-stroke epilepsy group (35.3% vs. 15.2%), with continuous seizure freedom for any time point after baseline in 29.4% of patients with post-stroke epilepsy compared to 12.1% in those without. Adverse events, particularly psychiatric TEAEs, were more frequent in the post-stroke epilepsy group at 3 months (13.6% vs. 5.8%).

In a subgroup analysis of 75 patients with post-stroke epilepsy from the BRIVAFIRST study, adjunctive BRV demonstrated effectiveness and tolerability over 12-month period.[64] By 12 months, 42.7% of patients achieved a ≥50% reduction in baseline seizure frequency, with a seizure freedom rate of 34.7%. The treatment discontinuation rate was low, with only 13.3% of patients stopping treatment due to insufficient efficacy (8.0%) or poor tolerability (5.3%). Adverse events, mostly mild, were reported in 20.3% of patients.

Overall, adjunctive BRV appears effective and well-tolerated in managing post-stroke epilepsy, showing promising seizure reduction and retention rates in real-world settings.

Brain tumor related epilepsy (BTRE)

BTRE is a frequent and often drug-resistant complication in patients with gliomas and other brain tumors. BRV has demonstrated potential in this setting, not only as an antiseizure medication but also through possible antitumor effects. *In vitro* studies using glioma cell lines showed that BRV exerts dose-dependent cytotoxic and anti-migratory effects, modulates microRNAs involved in cell cycle and migration, and does not affect the expression of key drug resistance proteins such as P-gp.[65]

Clinically, a retrospective multicenter study involving 33 patients with BTRE found that adjunctive BRV treatment significantly reduced monthly seizure frequency from 7.0 to 2.0 (p=0.001).[66] Adverse events occurred in 21.2% of patients, with psychiatric adverse events resulting in discontinuation in 9.0%. Despite these concerns, BRV showed favorable efficacy and was generally well tolerated.

Further evidence was provided by a subgroup analysis from the EXPERIENCE study, which included 68 patients with BTRE and 1,380 without.[51] BRV discontinuation rates were 39.7% in the BTRE group and 33.5% in the non-BTRE group, primarily due to lack of effectiveness or tolerability. At 12 months, ≥50% seizure reduction was achieved in 34.1% of BTRE patients compared to 37.0% in non-BTRE patients. Three-month seizure freedom was observed in 18.2% vs. 15.8%, continuous seizure freedom in 11.4% vs. 12.9%, and BRV retention in 65.7% vs. 71.5%, respectively. TEAE rates, including psychiatric and cognitive events, were similar across groups.

These findings suggest that BRV may provide both antiseizure and potential antineoplastic benefits in BTRE, warranting further prospective evaluation.

Traumatic brain injury-related epilepsy (TBIE)

In the EXPERIENCE study, a subgroup analysis of 1,448 patients (49 with TBIE and 1,399 without) evaluated the effectiveness and tolerability of BRV.[51] At 12 months, ≥50% seizure reduction was achieved in 50.0% of patients with TBIE compared to 36.4% without. Seizure freedom at 3 months was 17.2% in the TBIE group vs. 15.9% in the non-TBIE group, and continuous seizure freedom was achieved in 13.8% vs. 12.8%, respectively. BRV retention was higher in the TBIE group (79.2%) compared to the non-TBIE group (70.9%), with fewer discontinuations due to TEAEs. No psychiatric, cognitive, or behavioral TEAEs were reported among TBIE patients during follow-up, supporting the favorable tolerability of BRV in this subgroup. Given the small sample size, these findings should be interpreted with caution, and further research is needed to validate the observed trends.

Pregnancy

BRV's effects in pregnant women remain largely unstudied. Therefore, BRV should be prescribed during pregnancy only if the benefits to the mother outweigh the potential risks to the fetus. Additionally, as BRV is excreted into breast milk and may result in measurable infant exposure, the decision to continue breastfeeding should be made after careful consideration of the benefits of treatment for the mother and the potential risks for the infant.[67,68]

The use of BRV in human pregnancy should be approached with caution due to the lack of sufficient research.

BRV usage in an acute setting

A phase II, open-label, randomized study assessed the efficacy and safety of intravenous BRV compared to lorazepam for acute seizure treatment within 30 minutes of a qualifying seizure in 45 patients in epilepsy monitoring unit.[69] Within 12 hours, seizure freedom rates were 60.0% for lorazepam doses 1 mg to 4 mg (median, 1 mg), 80.0% for BRV 100 mg, and 80.0% for BRV 200 mg. The use of rescue medication was higher in the lorazepam group (40.0%) than in BRV 100 mg (6.7%) and BRV 200 mg (13.3%). Although this study included a small number of patients and used median 1 mg of lorazepam, a dose lower than the therapeutic range, it nevertheless suggests that BRV may have a potential role in the acute management of increased seizure activity. A retrospective multicenter study by Orlandi et al.[70] evaluated the effectiveness and safety of intravenous BRV in the treatment of status epilepticus among 56 adult patients across multiple Italian centers. Status epilepticus etiologies included acute symptomatic (46.0%), remote (18.0%), and progressive symptomatic (16.0%), with 80% of cases presenting prominent motor features. BRV was administered as the first drug after benzodiazepine failure in 21%, and as the second or third-or-later drug in 38% each. The median loading dose was 100 mg (range, 50-300 mg). BRV was effective in 32 patients (57.0%), with early response (within 6 hours) documented in 22 patients (39.0%). Notably, BRV use within 6 hours of status epilepticus onset was strongly associated with early resolution (odds ratio, 32.0; 95% CI, 3.39-202; p=0.002). No severe TEAEs were reported, supporting the safety and early-phase efficacy of intravenous BRV in status epilepticus treatment.

A retrospective multicenter study conducted by the same group evaluated the effectiveness and safety of intravenous BRV for treating seizure clusters in 97 patients across 25 Italian neurology units between 2019 and 2022.[71] Results indicated that 58% of patients were seizure-free at 24 hours following BRV administration, with no additional rescue medications required in 77% of cases. Seizure clusters progressed to status epilepticus in 17% of patients, with a higher risk observed in those without a history of epilepsy or when BRV was used as a second- or third-line treatment. No severe adverse events were reported, suggesting that BRV is a viable option for treating seizure clusters in hospital settings.

These findings suggest that intravenous BRV may be an effective and safe alternative to traditional benzodiazepines for acute seizure management, with potential advantages in seizure control and adverse event profiles. Larger controlled studies are needed to confirm these findings and guide their integration into clinical practice.

Dose and administration

BRV dosing is individualized based on the patient's weight, therapeutic needs, and tolerability. It is available in multiple formulations to suit diverse clinical requirements, including oral film-coated tablet as 10, 25, 50, 75, and 100 mg, an oral solution as 10 mg/mL, and an intravenous preparation as 50 mg/5 mL. The oral solution can be diluted in water or juice before ingestion and administered with or without food. For patients needing tube administration, it can also be delivered via a nasogastric or gastrostomy tube. BRV is administered twice daily in equally divided doses, approximately 12 hours apart.

In a pooled analysis of three phase III trials (n=1,160), patients received BRV 50, 100, or 200 mg/day without up-titration following an 8-week baseline period and were treated for 12 weeks (84 days).[72] Sustained ≥50% responder status from day 1 was achieved by 15.5%, 18.1%, and 19.4% of patients in the 50, 100, and 200 mg/day groups, respectively, compared to 6.7% in the placebo group (p<0.001). BRV demonstrated a favorable tolerability profile and sustained efficacy from the first day of treatment, allowing initiation at the target dose without the need for up-titration. These findings support the early onset of BRV's therapeutic effect and confirm that full-dose initiation is both effective and well tolerated from the outset.

For adults aged 16 years and older, the recommended initial dose is 50 mg twice daily (100 mg/day), suitable for monotherapy or adjunctive therapy. Based on therapeutic response and tolerability, the dose can be adjusted within the range of 25 mg twice daily (50 mg/day) to 100 mg twice daily (200 mg/day). Dose modifications should be made carefully, considering the individual patient's needs and response.

For special populations, older patients (65 years and older) do not require dose adjustments; however, clinical data for this group are limited. In patients with renal impairment, dose modifications are generally unnecessary, except for those with end-stage renal disease undergoing dialysis, in whom BRV use is not recommended because of the lack of available data. Patients with hepatic impairment may require dose adjustments due to increased BRV exposure associated with liver dysfunction.

This flexible dosing regimen and the variety of formulations ensure that BRV can be tailored to meet the unique needs of each patient.

Conclusion

BRV demonstrates a favorable efficacy and safety profile across diverse clinical settings, ranging from adjunctive therapy in focal epilepsy to its use in special populations including older patients and those with post-stroke epilepsy.

Its unique pharmacological properties, including selective high-affinity binding to SV2A, rapid brain penetration, and favorable pharmacokinetics, set it apart from other antiseizure medications. Evidence from clinical trials and real-world studies underscores BRV's ability to achieve significant seizure reductions, high retention rates, and good tolerability.

Special populations, such as older patients, have demonstrated promising outcomes with BRV, achieving high seizure freedom rates while maintaining a good safety profile. Moreover, BRV's potential role as an acute seizure management option, particularly in hospital settings, underscores its versatility in addressing diverse clinical needs. Future research should prioritize long-term studies in special populations and expand its evaluation in generalized epilepsy and acute seizure management.

Overall, BRV offers a well-tolerated and effective treatment option for epilepsy management. Its unique pharmacological characteristics, clinical flexibility, and favorable safety profile establish it as a valuable addition to the range of available antiseizure medications, addressing several unmet needs in epilepsy treatment.

Conflicts of Interest

None.

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