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Pharmacy

AN OBSERVATIONAL STUDY ON UTILIZATION PATTERN OF BRIVARACETAM IN THE TREATMENT OF EPILEPSY

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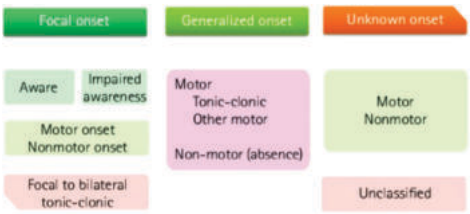
ABSTRACT A prospective observational study was done within 6 months, 30 participants aged 18 to 65 with partial-onset seizures, either with or without generalization were selected with the aim to observe the utilization pattern of Brivaracetam in the treatment of Epilepsy. Approximately 57% of the patients in the study were male, while the remaining 43% were female. Most patients who were prescribed Brivaracetam fell within the 51-65 age group. Out of the total number of patients, 20 were admitted for epilepsy-related reasons, while the remaining 10 patients were admitted for unrelated epilepsy issues. In terms of the administration of Brivaracetam, 50% of patients received the IV formulation at a dosage of 100 mg twice daily during their hospital stay. For patients who received the oral formulation, 53% were administered a dosage of 50 mg twice daily. Additionally, 27% of patients were solely treated for epilepsy with Brivaracetam, while 73% received it for seizure prevention. Out of the 30 patients, 63% received only Brivaracetam, while the remaining 37% received a combination of Brivaracetam and other AEDs. As for discharge medication, the most frequently prescribed form of Brivaracetam was a dosage of 50 mg orally twice a day, given to 15 out of 30 patients.

KEYWORDS : Brivaracetam, Epilepsy, Monotherapy, Neurological disorder, Prophylactic.

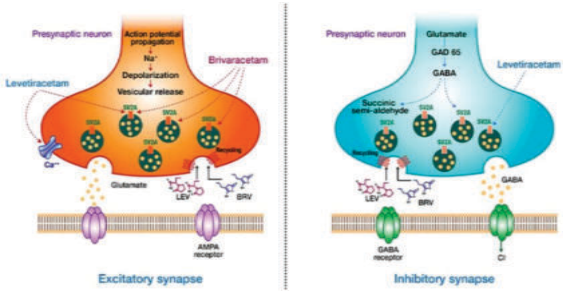
I. INTRODUCTION:

Epilepsy is a neurological disorder characterised by the reoccurrence of seizures. They are very sudden and may make some brief changes in the brain's neuronal activity. As it is a chronic condition it can be managed effectively by antiepileptics but cannot cured completely. The reports according to WHO was around 50-65 million have Epilepsy around the globe. The prevalence may vary across the regions and the countries and it suggests that around 0.6% to 1.5% global population has active Epilepsy. In India the frequency varies from 0.3 to 11.9 per 1000 people. Some research says that the focal seizures outnumber the generalised seizures. Common types of Epilepsy include: 1. Focal Epilepsy or partial Epilepsy 2. Generalised Epilepsy 3. Unknown onset Epilepsy.



Brivaracetam:

A propyl analogue of **Levetiracetam** which comes under the drug class called anti-convulsant that completed its stage III trial results in the year 2008 which were recorded with evidence that it is 10times more potent to supress or prevent the seizures in the animal models than Levetiracetam. It got its first approval on Jan14th 2016 by the European commission and on Feb18th by the U.S. Food and Drug Administration and the Drug Enforcement Administration (DEA) added this drug in the schedule V of the controlled substances act (CSA) by placing its interim final rule that is effective from march 9th of 2016 Canada had approved. The mechanism of action is not fully understood but it is believed to exert its antiepileptic effects by binding SV2A, a protein involved in the regulation of neurotransmitter release in the brain.



Pharmacokinetics Parameters	BRIVARACETAM	LEVETIRACETAM
Dosage formulations: Oral Intravenous	25mg, 50mg, 75mg,100mg 50mg/5mL	250mg, 500mg, 750mg, 1000mg 500mg/5ml,500mg/100ml,1500mg/5ml
Bioavailability	100% (may be delayed with high fat meal)	>95%
Time to Peak, median (range)	2 hour (1-4 hrs)	1 hour (1-2 hrs)
Protein binding	15-20%	<10%
Metabolism	Hydrolysis-primary metabolism Hydroxylation Unchanged-9%	34% metabolized (Hydrolysis) 66% unchanged

Involvement of CYP450 enzymes	Yes (CYP2C19)	No
Elimination half-life (t1/2)	7-8 hours	6-8 hours
Time for steady state	2 days of repeated dosing	24-48 hrs of repeated dosing
Clearance	95% via kidney (8-10% unchanged)	100% via kidney (66% unchanged)
Dose adjustment in renal failure/dialysis	Not required	Required (50% supplemental dose following HD)
Dose adjustment in liver failure	Reduce dose by 1/3 may be needed	Not required
Relevant drug-drug interaction	Reduced by co-administration of rifampin Reduce combined OCP's by 20-30% at 400mg/day	None

Abbreviations:
HD-Hemodialysis; CYP450- cytochrome P450; OCP- Oral contraceptive pills

II. AIMS AND OBJECTIVES:

- To study the utilization patterns of Brivaracetam in the treatment of epilepsy.
- To gain knowledge on its significant contribution of enhancing the effects of other anti-epileptic drugs while displacing levetiracetam
- To study the prescribed indications.
- To know the dose, dosage formulation and frequency.

Inclusion criteria:

- Age above 18 years and below 65 years.
- Outpatients and Inpatients.
- Patients with partial on-set of seizures with or without generalization.
- Patients prescribed with Brivaracetam (oral or intravenous form).

Exclusion criteria:

- Age below 18 years.
- The population with no history of seizures.
- Patients with comorbidities such as depression, alcoholism.
- Pregnancy and breastfeeding women.
- Geriatric patients (>65 years)
- Patients using Apalutamide, Ethanol, Fosphenytoin, Isoniazid, Rifampin, Pyrazinamide.

III. METHODOLOGY:

This is a randomised pilot study which was conducted for 6 months in Hyderabad from 24th December 2022 to 25th May 2023 in a tertiary care hospital.

30 subjects who experienced partial-onset of seizures were included in the study. The exclusion criteria of our study were those under 18, individuals with no history of seizures, those with specific medical conditions (depression, alcoholism), pregnant or lactating women, older patients, and those using certain medications (Apalutamide, Ethanol, Fosphenytoin, Isoniazid, Rifampin, and Pyrazinamide). The study aimed to determine the appropriate Brivaracetam dosage, formulation, frequency, concurrent anti-epileptic medications, and its indications. It was analysed by using MS-Excel tool which showed its efficacy as a monotherapy, despite primarily being used as a prophylactic medication. The study focused on individuals receiving Brivaracetam orally or intravenously.

IV. RESULTS AND DISCUSSION

The following are the results acquired from the 30 patients

Table 1: Distribution of Patients based on Gender:

Gender	No. of Patients	Percentage
Male	17	57
Female	13	43
Total	30	100

Demographic details:

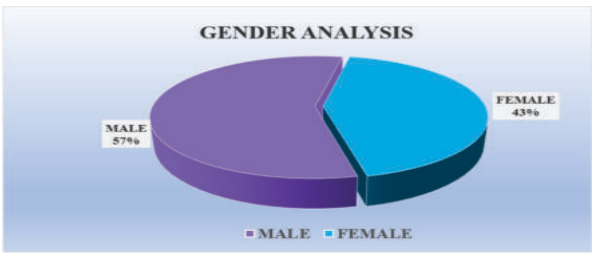


Figure 1: Pie chart representing the distribution of patient's based on Gender

Figure 1: explains the gender distribution in patients administered with Brivaracetam. This figure illustrates that a total of 30 patients were included in this study, out of which 57% were male and 43% were female.

Table 2 Distribution of patients based on Age

Age groups	No. of Patients
18-28	5
29-39	3
40-50	9
51-65	13

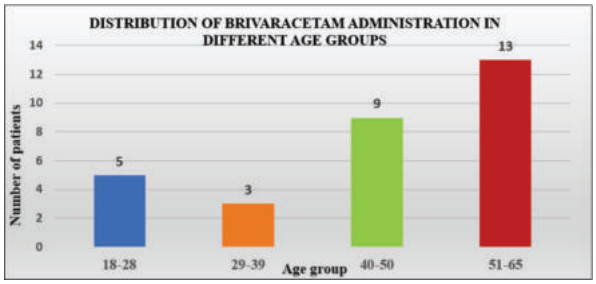


Figure 2: Bar graph representing the distribution of patients based on Age

Figure 2: explains the age distribution of Brivaracetam administration in different age groups. We have included patients above the age of 18 and below 65 years in this study. The figure illustrates that the number of patients in the age group 18-28 were 5, in the age group 29-39 were 3, in the age group 40-50 were 9 and 51-65 were 13.

Distribution of patients admitted due to Epilepsy related and unrelated reasons

Table 3: Distribution of Patients admitted due to Epilepsy related and unrelated reasons

Epilepsy related reasons	Epilepsy unrelated reasons
20	10

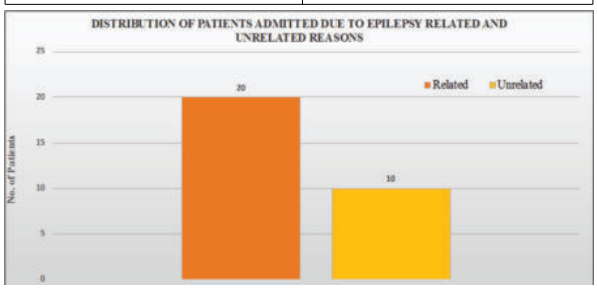


Figure 3: Bar graph representing patients admitted due to Epilepsy related and unrelated reasons

Figure 3: shows the reasons for admission of patients due to Epilepsy related and unrelated reasons. The bar graph shows that 20 patients were admitted due to epilepsy related reasons whereas 10 patients were admitted due to unrelated reasons such as slip and falls, meningioma, cancer, encephalopathy, stenosis, etc.

Distribution of patients admitted with or without a history of seizures

Table 4: Distribution of patients admitted with or without a history of seizures

Patients with history of seizures	Patients without a history of seizures
11	19

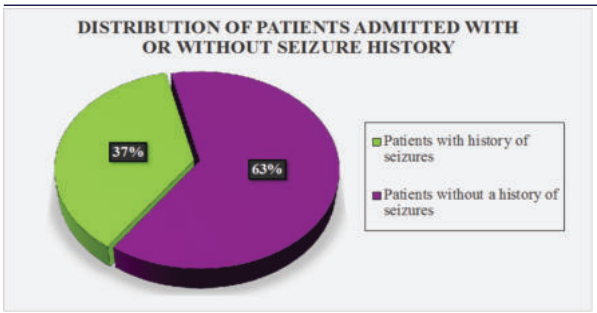


Figure 4: Pie chart representing patients with or without seizure history.

Figure 4: shows the distribution of patients admitted with or without a history of seizures. The pie chart represents that 63% of the patients did not have a history of seizures, whereas 37% of the patients had a history of seizures in the past.

Dose, Dosage form and Frequency of Brivaracetam administered to the patients

Table 5: Distribution of patients administered with IV formulation of Brivaracetam during hospital stay

Dose	Frequency	No. of Patients	Percentage
100 mg	BD	9	47%
50 mg	BD	8	42%
50 mg	OD	1	5%
75 mg	BD	1	%

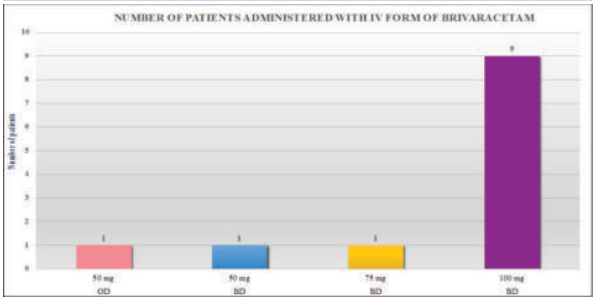


Figure 5: Bar graphs representing distribution of patients administered with IV formulation of Brivaracetam.

Figure 5: shows the distribution and number of patients administered with IV formulation of Brivaracetam during their hospital stay. The bar graph shows that 1 patient was administered with 50mg OD, 1 patient was administered with 50 mg BD, 1 patient was administered with 75 mg BD, 9 patients were administered with 100 mg BD. Highest number of patients were administered with 100 mg BD.

Table 6: Distribution of patients administered with oral formulation of Brivaracetam during hospital stay.

Dose	Frequency	No of patients
25 mg	BD	1
50 mg	OD	1
50 mg	BD	10
75 mg	BD	2
100 mg	BD	3
150 mg	BD	1

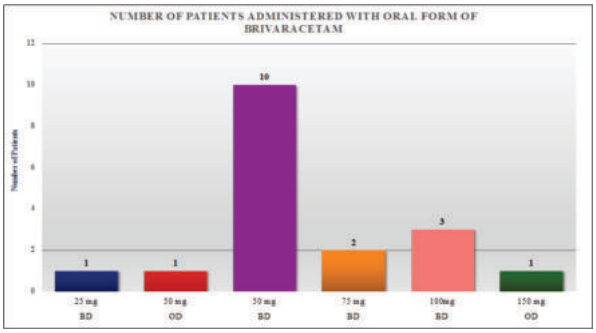


Figure 6: Bar graph representing distribution of patients administered with Oral formulation of Brivaracetam.

Figure 6: shows the distribution and number of patients administered with Oral formulation of Brivaracetam during their hospital stay. The bar graph shows that 1 patient was administered with 25 mg BD, 1 patient was administered with 50 mg OD, 10 patients were administered with 50 mg BD, 2 patients were administered with 75 mg BD, 3 patients were administered with 100

Table 7: Distribution of Brivaracetam usage based on diagnosis.

BRIVARACETAM FOR EPILEPSY TREATMENT	BRV FOR PROPHYLACTIC TREATMENT
8	22

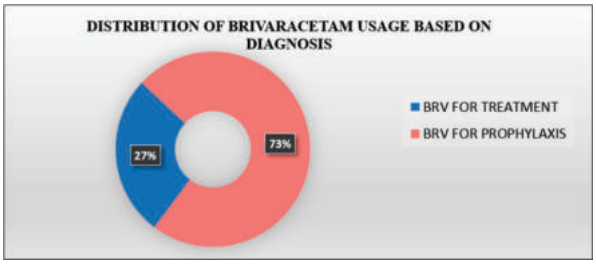


Figure 7: Pie chart representing distribution of Brivaracetam usage based on diagnosis.

Figure 7: shows the distribution of Brivaracetam usage during hospital stay based on diagnosis. The pie chart depicts that 27% of the patients were administered with Brivaracetam for Epilepsy treatment and reduction of seizure frequency and intensity, whereas 73% of the patients were given Brivaracetam for prophylaxis or prevention of seizures for various reasons such as Hemiparesis, Meningioma, Stenosis, Meningitis, Encephalopathy, Metastasis, TB, etc.

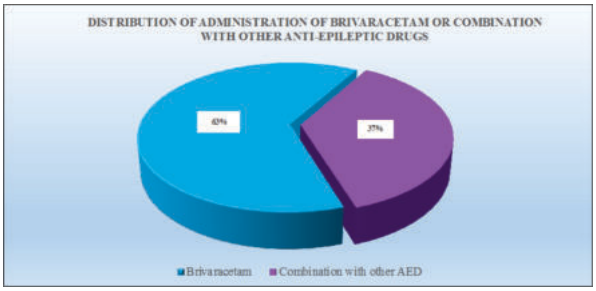


Figure 8: Pie chart representing distribution of administration of Brivaracetam or as Combination with other anti-epileptic drugs.

Figure 8: shows the distribution of administration of Brivaracetam or as a combination with other anti-epileptic drugs. 63% of the patients were administered with only Brivaracetam as a monotherapy, and 37% of the patients were given Brivaracetam along with other anti-epileptic drugs as combination therapy.

Table 9: Distribution of administration of Brivaracetam or as Combination with other anti-epileptic drugs.

Brivaracetam	Combination with other AED
19	11

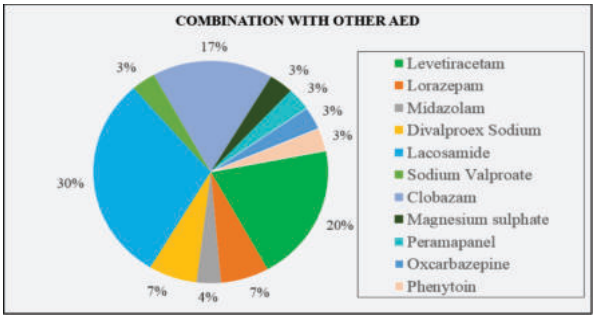


Figure 9: Pie chart representing distribution of other anti-epileptic drugs used as combination with Brivaracetam.

Figure 9: shows the distribution of other anti-epileptic drugs used as combination with Brivaracetam. The pie chart depicts that 20% of the patients were administered with Levetiracetam, 7% with Lorazepam,

4% with Midazolam, 7% Divalproex sodium, 30% with Lacosamide, 3% with Sodium Valproate, 17% with Clobazam, 3% with Magnesium sulphate, 3% with Peramapanel, 17% with Oxcarbazepine, and 3% with Phenytoin. The most frequently used AED is Lacosamide which was administered to 30% of the patients followed by Levetiracetam to 20% of the patients.

Table 10: Distribution of Brivaracetam prescribed as Discharge medication

Dosage form	Dose	No. of Patients	Percentage
PO	50 mg	15	50%
PO	75 mg	1	3%
PO	100 mg	8	27%
IV	10 mg	1	3%
IV	50 mg	1	3%
IV	100 mg	1	3%
Naso	100 mg	1	3%
PEG	50 mg	1	3%

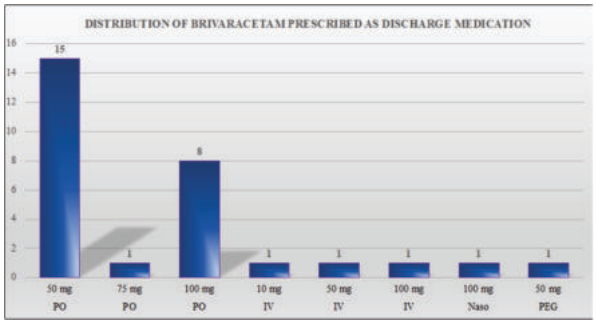


Figure 10: Bar graph representing the distribution of Brivaracetam prescribed as a discharge medication

Figure 10:
shows the distribution of Brivaracetam prescribed as discharge medication. The bar graph represents that 15 patients were prescribed with 50mg PO, 1 patient with 75 mg PO, 8 patients with 100 mg PO, 1 patient with 10 mg IV, 1 patient with 50 mg IV, 1 patient with 100 mg IV, 1 patient with 100 mg Naso, and 1 patient with 50 mg PEG. From this illustration, it's seen that highest number of patients were prescribed with 50 mg PO during discharge.

V. CONCLUSION

Brivaracetam exhibited its effectualness as a monotherapy, despite primarily being used as a prophylactic medication. Moreover, it was well-tolerated by most patients when administered as a single agent, without the need for combination therapy. The most frequently prescribed dose of Brivaracetam was 50 mg orally, which demonstrated good tolerability and effective seizure control. Hence, it suggests that Brivaracetam can serve as an effective option for preventing seizure recurrence in diverse clinical scenarios, either as a standalone treatment or in combination with other antiepileptic drugs (AEDs). In conclusion, this study provides valuable evidence supporting the effectiveness of Brivaracetam in epilepsy treatment. Still, more extensive investigations are warranted to strengthen these findings and optimize their usage in clinical practice.

REFERENCES:

1. J Zelano, M Holtkamp, N Agarwal, S Lattanzi, E Trinka, F Brigo: How to diagnose and treat post-stroke seizures and epilepsy Epileptic Disord, 22 (2020)
2. Gajanan Vithoba Panchal Vijay Nath mishra: A brief review on efficacy and safety of brivaracetam in the management of partial onset epilepsy
3. Rebecca Bresnahan, Mariangela Panbianco, Anthony G Marson: Brivaracetam add.on therapy for drug. resistant epilepsy
4. Anteneh M Feyissa: Brivaracetam in the treatment of epilepsy: a review of clinical trial data 2019 Volume 2019:15 pages 2587-2600
5. Pavel Klein, Anyzeila Diaz, Teresa Gasalla & John Whitesides: (2018) A review of the pharmacology and clinical efficacy of brivaracetam, Clinical Pharmacology: Advances and Applications, , 1-22
6. Mumoli L, Palleria C, Gasparini S, Citraro R, Labate A, Ferlazzo E, Gambardella A, De Sarro G, Russo E Brivaracetam: review of its pharmacology and potential use as adjunctive therapy in patients with partial onset seizures 2015
7. Ferlazzo E, Russo E, Mumoli L, Sueri C, Gasparini S, Palleria C, Labate A, Gambardella A, De Sarro G, Aguglia U Profile of brivaracetam and its potential in the treatment of epilepsy Neuropsychiatric Disease and Treatment 2015
8. Mumoli L, Palleria C, Gasparini S, Citraro R, Labate A, Ferlazzo E, Gambardella A, De Sarro G, Russo E : Brivaracetam: review of its pharmacology and potential use as adjunctive therapy in patients with partial onset seizures Drug Design, Development and Therapy 2015,
9. Kuan-Ying Li, Chung-Yao Hsu, Yuan-Han Yang : cognitive and behavioral outcomes of Brivaracetam
10. Isabella Lince-Rivera , Natalia Martínez Córdoba , Johann Sebastián Ortiz De la Rosa : brivaracetam for genetic generalized epilepsies
11. Stephan Arnold [a], Cédric Laloyaux [b], AnneLiv Schulz [c], Sami Elmoufti [d], Stephen Yates [d], Toufic Fakhoury [e] : Long-term safety and efficacy of brivaracetam in adults with focal seizures Volume 166, October 2020,
12. Madhuri Khilari, Pradeep P Nair, Brajesh Kumar Jha : Brivaracetam: How Well Does It Fare as an Anti-Epileptic
13. Pavel Klein Ivana Tyrlikova Milan Brazdil Ivan Rektor : Brivaracetam for the treatment of epilepsy Pages 283-295
14. Victor Biton, Samuel F. Berkovic, Bassel Abou-Khalil, Michael R. Sperling , Sarah Lu : Brivaracetam as adjunctive treatment for uncontrolled partial epilepsy in adults
15. Yamane Makke Bassel Abou-Khalil Brivaracetam efficacy and safety in focal epilepsy Pages 955-964
16. Christian Brandt a, Pavel Klein b, Vincent Badalamenti c, Teresa Gasalla c, John Whitesides c: Safety and tolerability of adjunctive brivaracetam in epilepsy: In-depth pooled analysis
17. Linda J. Stephen and Martin J. Brodie: Brivaracetam: a novel antiepileptic drug for focal-onset seizures Therapeutic Advances in Neurological Disorders Volume 11, January-December 2018
18. Sebastian F Grenn Green, Nisha Hare, Mehreen Kassam, Fergus Rugg-Gunn, Matthias J. Koepp, Josemir W. Sander, Sanjeev Rajakulendran: Retention of brivaracetam in adults with drug-resistant epilepsy, Published: August16,2022
19. Manuel Toledo [a], Christian Brandt [b], Pier Paolo Quarato [c], Anne-Liv Schulz [d], Jody M. Cleveland [c], Gilbert Wagener [d], Pavel Klein : Long-term safety, efficacy, and quality of life during adjunctive brivaracetam treatment in patients with uncontrolled epilepsy : Epilepsy & Behavior Volume 118, May 2021
20. V. Biton, S.F. Berkovic, B. Abou-Khalil, M.R. Sperling, M.E. Johnson, S. Lu: Brivaracetam as adjunctive treatment for uncontrolled partial epilepsy in adults: A phase III randomized, double-blind, placebo-controlled trial Epilepsies, 55 (2014)
21. C. Brandt, P. Klein, V. Badalamenti, T. Gasalla, J. Whitesides: Safety and tolerability of adjunctive brivaracetam in epilepsy: In-depth pooled analysis: Epilepsy Behave, 103 (2020)
22. P. Klein, J. Schiemann, M.R. Sperling, J. Whitesides, W. Liang, T. Stalvey: A randomized, double-blind, placebo-controlled, multicenter, parallel-group study to evaluate the efficacy and safety of adjunctive brivaracetam in adult patients with uncontrolled partial-onset seizures: Epilepsia, 56 (2015)
23. P. Ryvlin, K.J. Werhahn, B. Blaszczyk, M.E. Johnson: Adjunctive brivaracetam in adults with uncontrolled focal epilepsy: Results from a double-blind, randomized, placebo-controlled trial Epilepsia
24. C. Brandt, P. Klein, V. Badalamenti, T. Gasalla, J. Whitesides: Safety and tolerability of adjunctive brivaracetam in epilepsy: In-depth pooled analysis: Epilepsy Behav, 103 (2020)
25. B.J. Steinhoff, M. Bacher, I. Bucurenciu, B. Hillenbrand, T. Intravooth, R. Kornmeier: Real-life experience with brivaracetam in 101 patients with difficult-to-treat epilepsy-A monocenter survey Seizure-Eur J Epilepsy, 48 (2017)
26. Isabella Lince-Rivera a, Natalia Martínez Córdoba a, Johann Sebastián Ortiz De la Rosa: Narrative review of brivaracetam for genetic generalized epilepsies
27. Brian D. Moseley a, Hugues Chanteux b, Jean-Marie Nicolas b, Cédric Laloyaux c, Barry Gidal d, Armel Stockis b:A review of the drug−drug interactions of the antiepileptic drug brivaracetam
28. Klein P, Diaz A, Gasalla T, Whitesides J: A review of the pharmacology and clinical efficacy of brivaracetam: Received 31 May 2017 Accepted for publication 23 August 2017 Published 19 January 2018 Volume 2018:10 Pages 1—22
29. A. Matagne, D.G. Margineanu, B. Kenda, P. Michel, H. Klitgaard: Anti-convulsive and anti-epileptic properties of brivaracetam (ucb 34714), a high-affinity ligand for the synaptic vesicle protein, SV2A Br. J. Pharmacol 154 (2008)
30. B.D. Moseley, C. Otoul, L. Staelens, A. Stockis: Pharmacokinetic interaction of brivaracetam on other antiepileptic drugs in adults with focal seizures: pooled analysis of data from randomized clinical trials Epilepsy Res., 158 (2019)
31. M.L.Sargentini-Maier, P. Espié, A. Coquette, A. Stockis: Pharmacokinetics and metabolism of 14C-brivaracetam, a novel SV2A ligand, in healthy subjects Drug Metab. Dispos., 36 (2008)
32. M.L. Sargentini-Maier, M.C. Homery, A. Stockis: Pharmacokinetics, safety and tolerability of brivaracetam in healthy elderly subjects : Epilepsia, 49 (Suppl. 7) (2008)