Summer Training at
UCB India Pvt ltd,
Mumbai

Perception Mapping of Customer Insights on Choice of Anti-Epileptic Drugs and Awareness About Brivaracetam

By
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MBA Pharmaceutical Management
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The IIHMR University, Jaipur
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INSTITUTE OF HEALTH MANAGEMENT RESEARCH
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IIHMR UNIVERSITY

CERTIFICATE

To Whomsoever It May Concern

This is to certify that **Ms. Akanksha Sharma,** student of MBA Pharmaceutical Management, from The IIHMR University, Jaipur has undergone Summer Training Project at **UCB India Pvt. Ltd., Mumbai** from **14th April to 14th June, 2016.**

The Candidate has successfully carried out the study designated to her during summer training and her approach to the study has been sincere, scientific and analytical. This training is in fulfillment of the course requirements.

I wish her success in all her future endeavors.

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June 30, 2016

TO WHOMSOEVER IT MAY CONCERN

This is to certify that Ms. Akanksha Sharma was appointed as "Trainee" with our organisation for a summer internship project from April 14, 2016.

Akanksha successfully completed her project titled 'Perception Mapping of Consumer Insights on choice of Anti-Epileptic drugs and awareness about Brivaricetam' on June 14, 2016.

We wish her success in all her future endeavours.

With Best Regards,

For UCB INDIA PRIVATE LIMITED

Sudip Chakraborty
Head - Neuro PVU & Commercial Operations

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Acknowledgment

"An endeavour over a period can be successful only with the advice and support of wellwishers. I take this opportunity to express my gratitude and appreciation to all those who encouraged me to complete this project.

At the beginning I would like to express my special gratitude and appreciation to **Mr. Deep Bhandari**, Head of Business Unit – Multiple Sclerosis at UCB & **Mr. Sudip Chakraborty**, Country Head – Neurology & Operations at UCB, for allowing me to pursue my summer training from UCB India Pvt Ltd, Mumbai.

I am extremely thankful and pay my gratitude to Project Mentor - **Mrs. Kanchan Waikole**, Product Manager, UCB India Pvt Ltd. for giving me this opportunity to learn and guidance.

I would like to express my deep sense of gratitude for my faculty mentor **Mr. Abhishek Dadhich**, Assistant professor, IIHMR University Jaipur and I am greatly indebted to them for providing their valuable guidance at all stages of the study, their advice, constructive suggestions, positive and supportive attitude and continuous encouragement.

To place on record, I owe a debt of gratitude to all my teachers for grooming me and my classmates for the inspiration needed to work with dedication and motivation throughout as an Intern at UCB India Pvt Ltd.

I would like to present Sincere thanks to the respondents for sparing their valuable support and providing relevant information. I hope that I can build upon the experience and knowledge that I have gained and make a valuable contribution towards the industry in coming future.

AKANKSHA SHARMA

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Executive Summary:

The Project assigned was "**Perception Mapping of Customer Insights On Choice of Anti-Epileptic Drugs & Awareness About Brivaracetam**" with primary objectives being:

✓ To identify and assess the usual Choice of Monotherapy in Partial Onset Seizures.
✓ To understand the Most Frequently Used Add-On in Partial Onset Seizures.
✓ To identify the Important Criteria for First Add-On in Partial Onset Seizures.
✓ To find the Awareness About Brivaracetam (new launch product) among Neurologist.

The project was carried out in 3 stages:

- First stage was to carry out the Doctors Survey to understand the First choice of Monotherapy & Frequently used Add-On in Mumbai.
- Second stage was to carry out the Doctors Survey to understand the First choice of Monotherapy & Frequently used Add-On in Delhi.
- Final stage was to move ahead with data analysis and conclusion.

The following results were obtained after the completion of the entire project-

1.At Delhi & Mumbai, the neurologist's choice of monotherapy was found that carbamazepine & sodium valproate i.e. first line drugs.

2.Most frequently used add-on prescribed by neurologist in partial epilepsy were found that Levetiracetam, Lacosomide & Clobazam.

3.According to neurologists, the most important criteria for first add-on therapy were Faster onset action, high seizure freedom rates & drug efficacy and safety.

4. In Mumbai & Delhi, total 70 neurologists were surveyed, among them approximately 41% of neurologists is aware about recently new launch Anti-epileptic drug i.e. Brivaracetam.

Company profile:

UCB(union chimique belge) is a multinational biopharmaceutical company headquartered in Brussels, Belgium. UCB is an international company with revenues of €3.3 billion that focuses primarily on R&D, specifically involving medications centered on Epilepsy, Parkinson's, & Crohn's diseases. The Company's efforts are focused on treatments for severe diseases treated by specialists, particularly in the fields of central nervous system (CNS) disorders (including epilepsy), inflammatory disorder (including allergy), and oncology.

Vision:

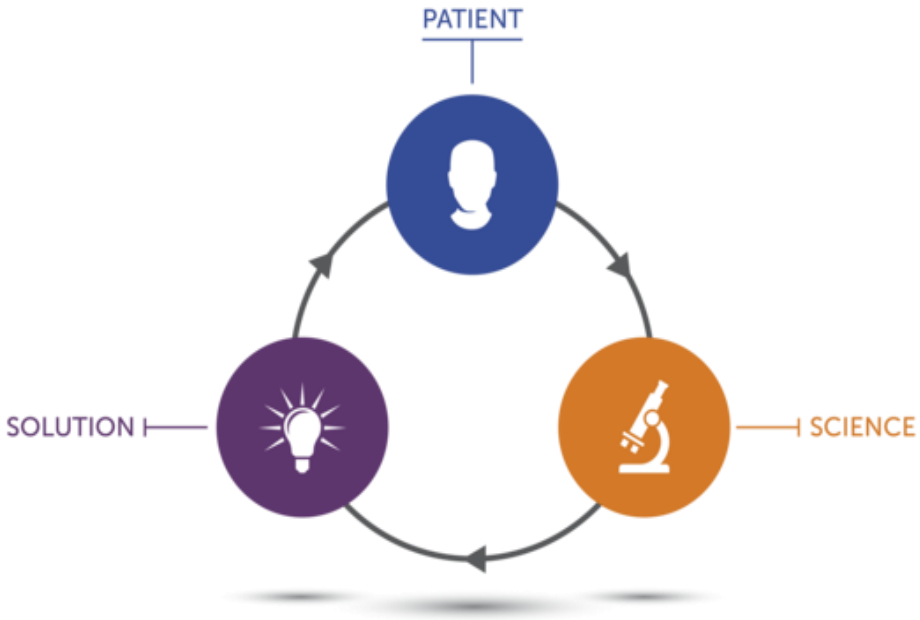
Everything we do starts with one simple question: “How can we create more value for people living with severe diseases?".

Notable drugs developed by UCB

- Atarax (hydroxyzine)
- Nootropil (Piracetam)
- Zyrtec (cetirizine), an OTC antihistamine.
- Keppra (levetiracetam), an anticonvulsant medication used to treat epilepsy.
- Xyzal (levocetirizine), a third-generation non-sedative antihistamine.
- Cimzia (certolizumab pegol), a monoclonal antibody to TNF-α for the treatment of Crohn's disease and rheumatoid arthritis.
- Neupro (rotigotine), a transdermal patch for treatment of Parkinson's disease.
- Vimpat (lacosamide), an anticonvulsant.
- Atamet® (Carbidopa/levodopa) for Parkinson's disease

Patient Value Strategy-

UCB aims to deliver differentiated and sustainable value to patients, which leads to increased value for UCB and its shareholders.



UCB's Patient Value Strategy is going beyond price-cost discussion, reflecting a shift from volume to patient value creation, striving for long-term patient value outcomes and integrates the patients' insight throughout our operating model. Innovation leads to differentiated medicines which secure future sustainability. A network approach strengthens external connections and digital solutions, focuses on competitive strengths and enables a true learning organization. UCB's value proposition as patient preferred biopharma is to deliver growth.

FLAGSHIP BRANDS-

Immunology

Cimzia® (certolizumab pegol)-Axial spondyloarthritis

Cimzia® (certolizumab pegol)-Crohn's disease

Cimzia® (certolizumab pegol)-Psoriatic arthritis

Cimzia® (certolizumab pegol)-Rheumatoid arthritis

Neurology

Briviact® (brivaracetam)-Epilepsy

Vimpat® (lacosamide)-Epilepsy

Keppra® (levetiracetam)-Epilepsy

Neupro® (rotigotine)-Parkinson's disease

Neupro® (rotigotine)-Restless legs syndrome

Introduction

Background

Epilepsy is a chronic medical disorder or condition, usually resulting in unpredictable, unprovoked recurrent seizures that affect a variety of mental and physical functions. It is one of the most common neurological diseases, affecting more than 3 million people in the India and about 50 million people worldwide. Epilepsy was one of the first brain disorders to be described. It was mentioned in ancient Babylon more than3,000 years ago. Through the ages, the strange behavior caused by some seizures has led to the creation of numerous superstitions and prejudices. The term epilepsy is derived from the Greek word *epilambanein*, meaning to attack or seize. A person is considered to have epilepsy when two or more unprovoked seizures occur that can't be explained by a medical condition such as fever or substance withdrawal. Seizure scan be the result of a family tendency toward the disease, or they can occur after a brain injury, but the cause of epilepsy is largely unknown. Epileptic seizures are manifested by an abnormal, excessive, and hypersynchronous electrical discharge of neurons in the brain. The characteristics of the AED as regards to efficacy and safety have led to therapeutic approaches based both on the analysis. This survey aims to summarize the experience of Neurologists in order to reveal a potential consensus on the modalities of therapeutic management for the first-line management of newly diagnosed epilepsy in adults or in cases of failure of first-line monotherapy.

The choice of an antiepileptic drug (AED) in patients with epilepsy is mainly based on efficacy and safety of each drug. However, these criteria of drug selection should be further evaluated according to the epileptic syndromes, and adjusted to the sex and age of the patient. Unfortunately, very few studies have been conducted based on these latter criteria. We conducted a survey on the management of epilepsy treatment. This survey was undertaken in Mumbai & Delhi, on anti-epileptic drug treatment in Partial onset seizures patients with newly diagnosed epilepsy. My survey suggests that there is a consensus among Neurologist for the choice of AEDs, mainly based on the epilepsy partial onset seizures. Gender also plays a crucial role. Sodium valproate and lamotrigine are the two drugs of choice for generalized epilepsies, as well as for undetermined epilepsies. Lamotrigine is often preferred for women of childbearing age. First line AEDs in partial epilepsy are carbamazepine (particularly for men), lamotrigine (particularly for women), and gabapentin (in the elderly). In cases of failure and/or intolerance to one of these AED, the principal alternatives are oxcarbazepine, sodium valproate and topiramate.

It is necessary to determine the type of seizure in order to focus the diagnostic approach on a particular etiologic factor, to select the appropriate drug therapy, to conduct scientific investigations that require delineation of clinical and EEG phenotypes, and to provide vital information regarding the prognosis. In 1981, the International League against Epilepsy (ILAE) published a modified version of the International Classification of Epileptic Seizures (ICES), which has continued to be a very useful system. This system is based on the clinical features of seizures and associated EEG findings. The etiology or cellular substrate is not considered. There are three main types of seizures: partial, generalized, and unclassified. A modified version of the ICES is presented in Table.

TYPES OF EPILEPTIC SEIZURES

Partial (focal) seizures
- Simple partial (with motor, sensory, autonomic, or psychic signs; consciousness is not impaired)
- Complex partial (consciousness is impaired)
- Partial seizures evolving to secondarily generalized seizures

Primarily generalized seizures
- Absence (petit mal)
- Myoclonic
- Clonic
- Tonic
- Tonic–clonic (grand mal)
- Atonic

Unclassified seizures
- Neonatal seizures
- Infantile spasms

Partial. Partial seizures are confined to discrete areas of the cerebral cortex; only a certain area of the body is usually involved, at least at the start. By contrast, generalized seizures are noted in diffuse regions of the brain. Simple partial seizures cause motor, sensory, autonomic, or psychic symptoms without an obvious alteration in consciousness. These seizures may also be manifested as changes in somatic sensation (e.g., paresthesias or tingling), vision, equilibrium, autonomic function olfactory changes, and hearing. Complex partial seizures are characterized by focal seizure activity, accompanied by transient impairment of the patient's ability to maintain normal contact with the environment. Partial seizures can spread to involve both cerebral hemispheres and may produce a generalized seizure, usually of tonic–clonic variety. Secondary generalization is often observed following simple partial seizures, especially those with a focus in the frontal lobe.

Generalized. Generalized seizures arise from both cerebral hemispheres simultaneously. Absence seizures (petit mal) are characterized by sudden, brief lapses of consciousness without loss of postural control. The seizure typically lasts for only seconds; consciousness returns as suddenly as it was lost, and there is no postictal confusion. Atypical absence seizures have features that deviate clinically and electro physiologically from typical absence seizures. For example, the lapse of consciousness is usually of longer duration and less abrupt in onset and cessation. A simple absence seizure is defined as a brief clouding of the sensorium, or loss of consciousness, accompanied by certain generalized epileptic discharges without other detectable clinical signs. A complex absence seizure indicates that other signs are also present. Generalized, tonic–clonic seizures (formerly grand mal) are the main seizure type in approximately 20% of all persons with epilepsy. They are also the most common seizure type resulting from metabolic derangements and are therefore frequently encountered in many different clinical settings. Atonic seizures are characterized by sudden loss of postural muscle tone lasting 1 to 2 seconds. Consciousness is briefly impaired, but there is usually no postictal confusion. Myoclonus is a sudden and brief muscle contraction that may involve one part of the body or the entire body.

Unclassified. Not all seizure types are partial or generalized; this appears to be true of seizures that occur in neonates and infants. Some of the seizures that occur in neonates and infants likely result, in part, from differences in neuronal function and connectivity in the immature brain.

ETIOLOGY

Seizures result from a shift in the normal balance of excitation and inhibition within the CNS as well as from abnormal brain function. Because various properties control neuronal excitability, it is not unusual that this normal balance can be disturbed in many different ways; thus, there are many causes of seizures and epilepsy. In about 70% of patients, no cause can be found. The normal brain is capable of experiencing a seizure under certain circumstances, and individuals vary in their susceptibility or threshold for seizures. Patients may have seizures intermittently, with periods of months to years between seizures. There are several possible causes of seizures in a given patient:

1. Seizures may be induced by a high fever in children who are otherwise healthy, who have a structural defect, or who have genetic risk factors.
2. A severe, penetrating head trauma or injury is associated with almost a 50% risk of subsequent epilepsy.
3. In older patients, Alzheimer's disease and stroke may precipitate epilepsy.

PATHOLOGY

Symptomatic epilepsy is associated with definable brain lesions. These lesions include zones of neuronal loss and gliosis (scars) or other signs of tissue loss. The frequency of occurrence of these lesions is not fully known. Epileptogenesis refers to the transformation of a normal neuronal network into one that is chronically hyperexcitable. There is a delay of months to years between an initial CNS injury such as trauma, stroke, or infection and the first seizure. The injury may lower the seizure threshold in the affected area until a spontaneous seizure takes place. In many genetic and idiopathic forms of epilepsy, epileptogenesis may be determined by developmentally regulated events A more complex genetic element is also identified in several childhood seizure disorders, for instance, (1) absence epilepsy with 3-per-second spike-and-wave discharges and (2) benign epilepsy of childhood with centrotemporal spikes. Both of these disorders are transmitted as autosomal dominant traits with incomplete penetrance, perhaps in a more complicated manner. Gene mutations observed in symptomatic epilepsy appear to be associated with pathways affecting CNS development or neuronal homeostasis. In patients with symptomatic epilepsy, other neurological abnormalities, such as cognitive impairment, coexist with seizures. The challenge is to identify the multiple susceptibility genes that underlie the more common forms of idiopathic epilepsy.

DIAGNOSIS

In the diagnosis of epilepsy, history is the key, because in most adults, the physical examination is relatively non definitive. The examination of infants and children is of greater value, because the presence of dysmorphic and cutaneous abnormalities allows for the diagnosis of a number of highly characteristic cerebral diseases that give rise to epilepsy. When a patient is seen shortly after a seizure, the first priorities are attention to vital signs, respiratory and cardiovascular support, and treatment of seizures if they resume. The physician's main means of diagnosis is to take a careful medical history, gathering as much information as possible about what the seizures looked like and what happened just before they began. The physician should also perform a thorough physical examination, especially of the nervous system, as well as an analysis of blood and other body fluids. Several laboratory studies are usually included in the initial diagnostic evaluation, such as a complete blood count, blood chemistry profiles, liver and thyroid function tests, an EEG, and a brain study, preferably with magnetic resonance imaging (MRI). Computed tomography (CT) scanning may be the only practical study in an emergency or for very young children. Some patients may later require video/EEG or prolonged EEG monitoring, either in the hospital or with portable equipment in the home.

MANAGEMENT

When a neurologist or a physician has made the diagnosis of seizures or epilepsy, the next step is to select the best form of treatment. If epilepsy (a continuing tendency to have seizures) is diagnosed, the neurologist usually prescribes seizure-preventing medications. If drugs are not successful, surgery, a special diet, complementary therapy, or vagus nerve stimulation may be tried. The goal of treatment is to prevent further seizures, avoid adverse effects, and enable patients to lead active lives.

Medical Treatment

Antiepileptic drug (AED) therapy, the mainstay of treatment for most patients, has four goals: to eliminate seizures or reduce their frequency to the maximum degree possible, to evade the adverse effects associated with long-term treatment, and to aid patients in maintaining or restoring their usual psychosocial and vocational activities, and in maintaining a normal lifestyle. The decision to start AED therapy should be based on an informed analysis of the likelihood of seizure recurrence, the consequences of continuing seizures for patients, and the beneficial and adverse effects of the pharmacological agent chosen. Whether to initiate therapy in a patient with a single seizure is controversial. A single seizure caused by an identified lesion

such as a CNS tumor, an infection, or trauma, in which there is strong evidence that the lesion is epileptogenic, should be treated. The overall goal of AED therapy is to prevent seizures completely. The relative risk of recurrence of epilepsy can vary, depending on the seizure type or syndrome. Patients with epileptic form discharges on an EEG or with congenital neurological defects are at high risk of recurrence (approaching 90%).13 The patient's and family's views should also be considered when AED treatment is begun. To prevent further seizures, it may be best to introduce AEDs early. Future seizure activity may be distressing for those who must drive, continue to work, or care for other family members. The probability of seizure recurrence varies among patients, depending on the type of epilepsy and any associated neurological and medical problems. Pharmacotherapy, however, carries a risk of adverse effects, at a rate approaching 30% after initial treatment. Treating children presents additional problems, especially on brain development, learning, and behavior, when a drug is used chronically.

ANTI-EPILEPTIC DRUGS

1.Levetiracetam

Levetiracetam is a broad spectrum AED which selectively inhibits high-voltage-activated calcium channels and reduces calcium release from intraneuronal stores. It also binds to a specific target in the brain, the synaptic vesicle protein 2A (SV2A), an integral membrane glycoprotein, which is involved in the control of vesicle fusion and exocytosis.

*Indication*s: Levetiracetam is effective as adjunctive therapy in pediatric patients with partial onset seizures and in primary generalized tonic-clonic seizures.
Intravenous preparation has recently shown efficacy in neonatal seizures and status epilepticus.

Efficacy: In a randomized, double-blind, placebo controlled, multicenter trial in 101 children with refractory partial seizures, >50% seizure reductions was seen in 44.6% receiving levetiracetam and 19.6% in patients receiving placebo. Levetiracetam has been evaluated in childhood epilepsy syndromes including rolandic epilepsy, electrical status epilepticus in slow sleep, myoclonic and tonic clonic seizures of Lennox Gastaut syndrome and as an alternative to valproate in juvenile myoclonic epilepsy in adolescent girls. Beneficial effects on language development have been reported.

Advantages: Levetiracetam has a favourable pharmacokinetic profile in terms of safety in patients with liver disease and minimal drug interaction with other AEDs.

Side effect: Levetiracetam is well tolerated in children with minor adverse events like headache, anorexia, and somnolence. However, there are concerns of behavioral side effects like aggression, emotional lability, oppositional behavior, and psychosis in children.
Dosage: Pediatric dose start from 10 mg/kg/day (divided twice daily) to be hiked by 10-20 mg/kg every two weeks to a maximum dose of 40-60 mg/kg/day.

2.Lacosamide

Lacosamide is a functionalized amino acid that selectively enhances slow inactivation of voltage-gated sodium channels, increasing the proportion of sodium channels unavailable for depolarization.

Indication: Lacosamide is used in children with refractory epilepsy with 30-50% of children having more than 50% reduction in seizure frequency.
Efficacy: Lacosamide is available in both oral and as an injection for intravenous preparation, which may have a role in status epilepticus. Pediatric experience with lacosamide has been limited [40]. Most of the available literature are retrospective data on small number of patients with an efficacy rate of 30-50%.

Side effect: Lacosamide is generally well tolerated with reports of irritability, oral tics, and prolonged crying as adverse effects in children.

3.Topiramate

Topiramate is a sulphamate substituted monosaccharide, a broad spectrum AED acting on voltage dependent sodium channels, enhancement of GABA, decrease in glutamate and inhibition of carbonic anhydrase.

Indications: Topiramate is a useful adjunct in refractory partial or generalized epilepsy and other epileptic syndromes.

Efficacy: Topiramate has demonstrated efficacy as an adjuctive therapy in partial epilepsy, intractable epilepsy, Lennox Gastaut syndrome , infantile spasms , generalized epilepsy of infancy and myoclonic–astatic epilepsy . Pooled data from two randomized, double-blind studies found that topiramate adjunctive therapy may be efficacious for juvenile myoclonic seizures in adults and children .

Side effects: Topiramate has good safety with no evidence of life threatening adverse effects or organ toxicity. The most frequently reported side effects are dizziness, mental slowing, somnolence, ataxia, impaired concentration and

confusion. Most of these are transient and observed during the initial weeks of therapy and can be reduced by slow titration of the dose. Anorexia and mild weight loss has been observed during the therapy. Other reported side effects include metabolic acidosis, nephrolithiasis, decreased sweating and resultant hyperthermia. Children on combination of topiramate and valproate should be monitored for signs of encephalopathy resulting from hyperammonemia.

Dosage: Pediatric dosage is 1-3 mg/kg/day (divided twice daily) hiked bi-weekly to 3-8 mg/kg/day.

4.Valproic Acid and Valproate Injection

Valproic acid is a carboxylic acid. Its chemical name is di-*N*propyl acetic acid, and the molecular weight is 144.

Indication and Mechanism of Action-

Valproic acid has been effective in partial and generalized seizures and is indicated as monotherapy and adjunctive therapy for complex partial seizures, which begin in a limited area of the brain. These seizures may occur either in isolation or in association with other types of seizures. The drug is also indicated for patients with simple and complex absence seizures and as an adjunctive therapy for patients with multiple seizure types, including absence seizures.

5. Carbamazepine

Carbamazepine is related to the tricyclic antidepressants (TCAs). The carbamyl moiety is essential for potent antiseizure activity. The chemical name is 5H-dibenz[*b, f*]azepine- 5-carboxamide, and the molecular weight is 236.27. The drug is not related to other antiseizure agents.

Indication and Mechanism of Action

Carbamazepine is indicated for use as an anticonvulsant drug. Evidence supporting its efficacy as an AED was derived from studies that enrolled patients with partial seizures with complex symptomatology (psychomotor, temporal lobe); generalized tonic–clonic seizures (grand mal); and mixed seizure patterns, including the latter two types or other partial or generalized seizures. Absence (petit mal) seizures do not appear to be controlled by carbamazepine.

6.Brivaracetam is an analogue of levetiracetam, which has been found useful in adults with photosensitive epilepsy, and as an adjunctive treatment in refractory partial-onset epilepsy. There is no pediatric experience till now.

Research Objective-

- To identify and assess the usual Choice of Monotherapy in Partial Onset Seizures.
- To understand the Most Frequently Used Add-On in Partial Onset Seizures.
- To identify the Important Criteria for First Add-On in Partial Onset Seizures.
- To find the Awareness About Brivaracetam (new launch product) among Neurologists.

Research Methodology-

Research design:

Exploratory study

Sampling design:

Sampling

Non probability purposive sampling

Sample population:

Consultants (Neurologists)

Sample area:

Mumbai & Delhi

Sample size:

Mumbai - 25 Respondents

Delhi – 45 Respondents

Total – 70 Respondents

Survey, Analysis & Interpretation

1.In partial onset seizures, usual choice of monotherapy (rate them 1 to 5).

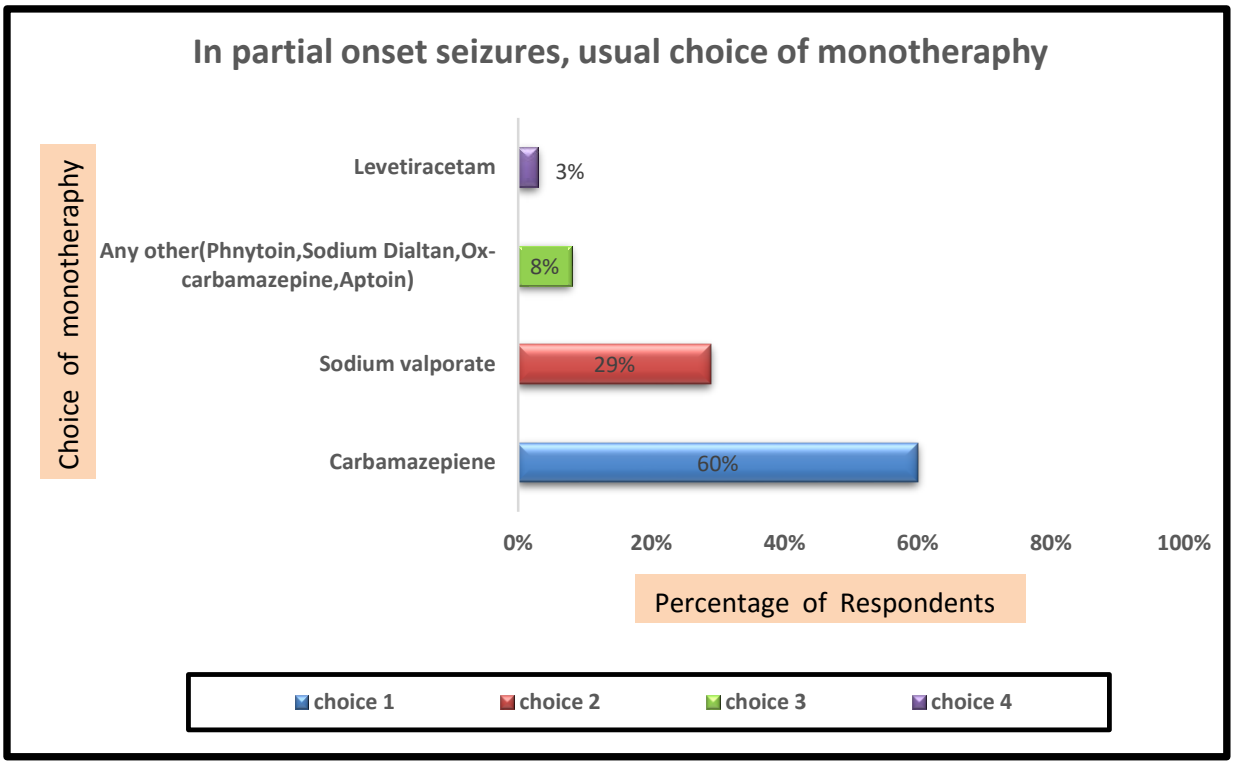


Figure 1-Shows the usual choice of monotherapy in partial onset seizures.

Interpretation-

It was found from the survey that first choice of monotherapy in partial onset seizures was Carbamazepine (60%) whereas second choice was sodium valproate (29%), reason being very minor side effects & cost effectiveness & its ease of availability however third choice of monotherapy includes Aptoin, Phnytoin, ox-carbamazepine sodium dialtan & fourth choice was found as levetiracetam (3%), alternative drug as choice of monotherapy.

2. Percent of patients in your practice do not respond to monotherapy in POS.

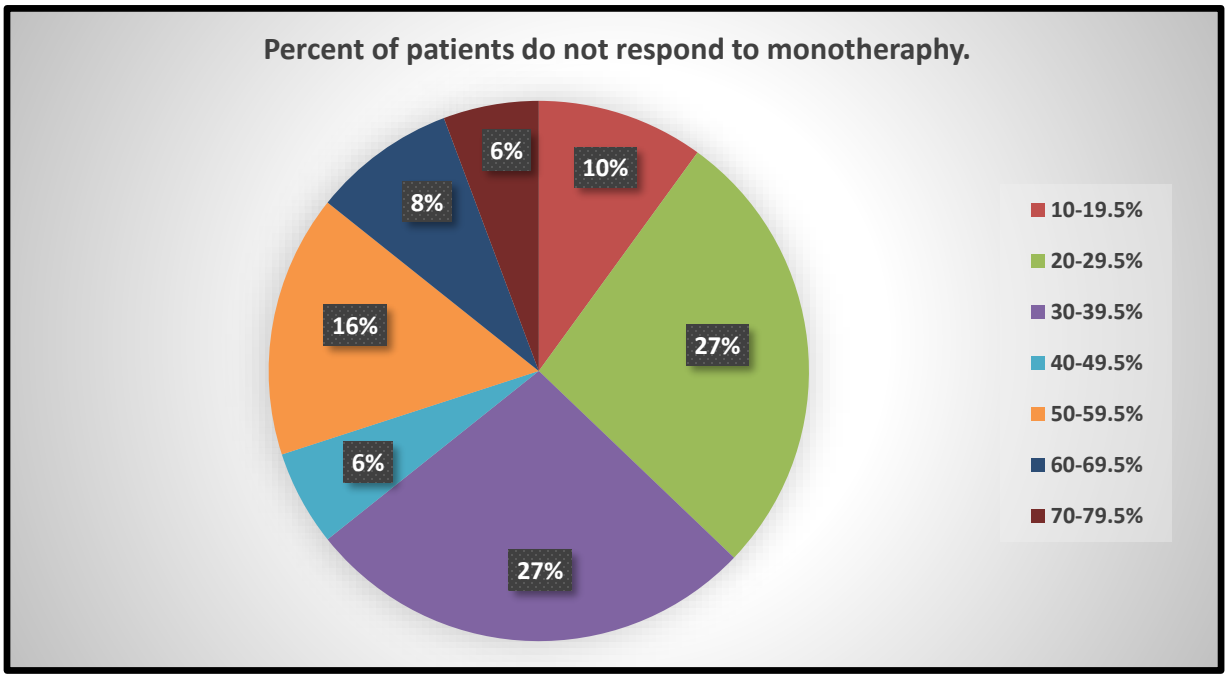


Figure 2-Shows the percent of patient which do not respond to monotherapy in POS.

Interpretation-

During study it was found that according to neurologists, in partial onset seizures, range between 20-40% of patients i.e 27% & 50-59.5%(16%) in their practice do not respond to monotherapy because some of became resistant from the first line drugs, sometimes due to lack of efficacy & adverse effect. In that case neurologists have two options, an alternative monotherapy (substitution) or a combination therapy (add-on).

3. The most frequently used add-on in POS.

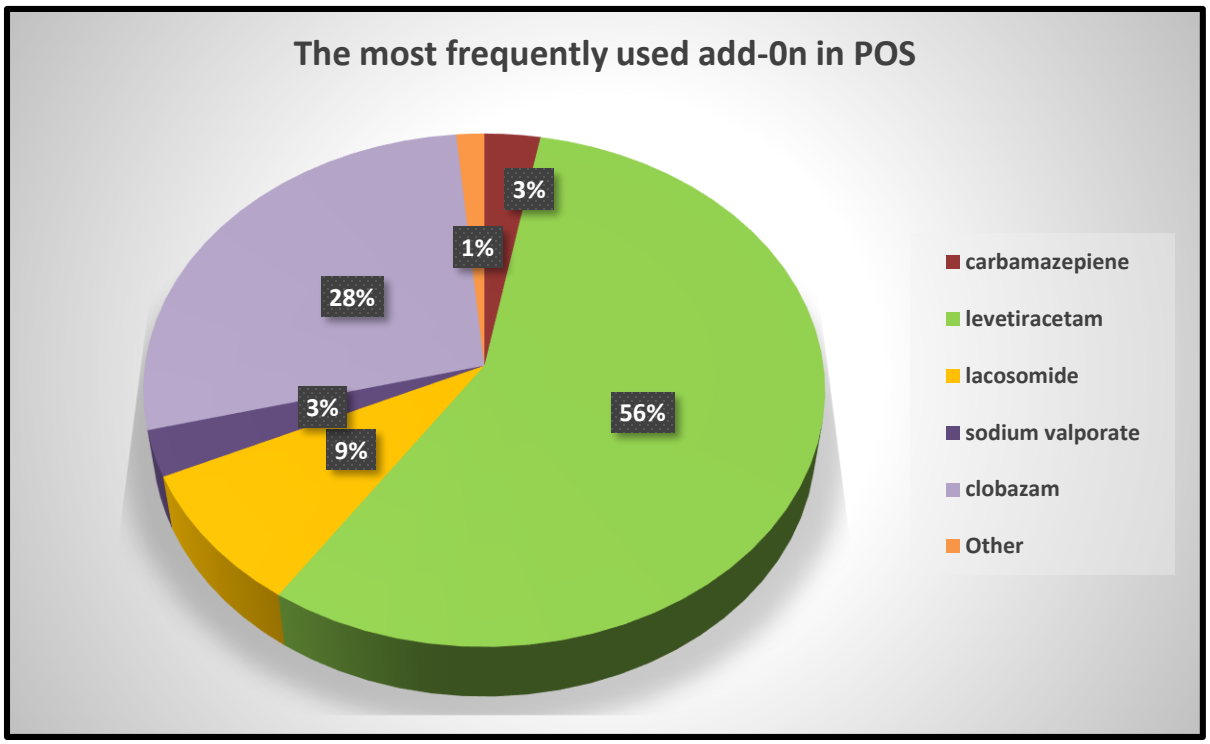


Figure 3-Shows the frequently used add-on in POS.

Interpretation-

It was found from the survey, out of 100% Neurologists ,56% of neurologists preferred Levetiracetam as a most frequently add-on in Partial onset seizures.While 9% & 28% preferred Lacosomide & Clobazam respectively however alternatives add-on with increasing dose & with some polytherapy are carbamazepine (3%) & sodium valproate(3%) .The add-on therapy included patients in whom a second Anti-epileptic drug was added to their current monotherapy.

4. **The most important criteria for ideal first add-on in POS.**

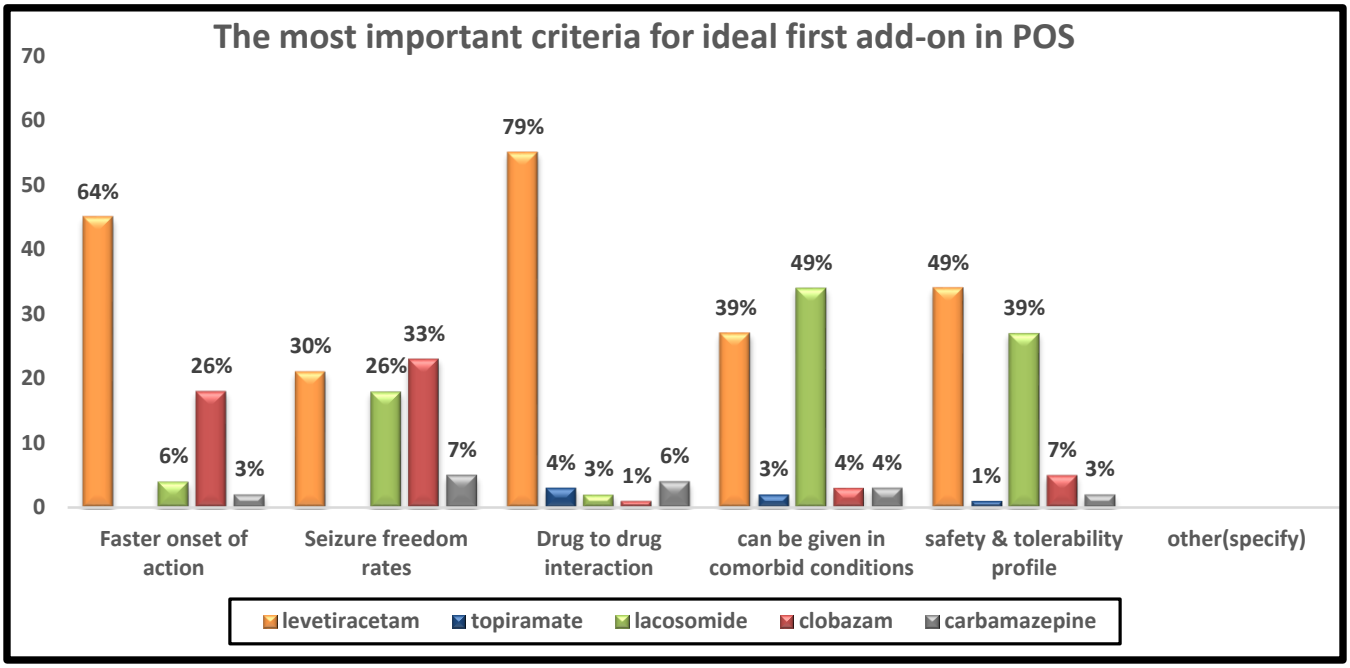


Figure 4-Shows the most important criteria for ideal first add-on in POS.

Interpretation-

1.It was found that, 64% of neurologists said **Levetiracetam** having faster onset of action & 79% said it having less drug to drug interaction ,39% said it can be given in comorbid conditions also & 49% said it has high safety & tolerability profile.

2.Out of 100% Neurologists,26% of neurologists said **Lacosomide** having high seizure freedom rates while 39% & 49% of neurologist said high safety & tolerability profile & also given in comorbid conditions respectively.

3.Out of 100% Neurologists,33% of neurologists said **Clobazam** having more seizure freedom rates while 26% said it has a faster onset of action.

5. **Are you aware about Brivaracetam?**

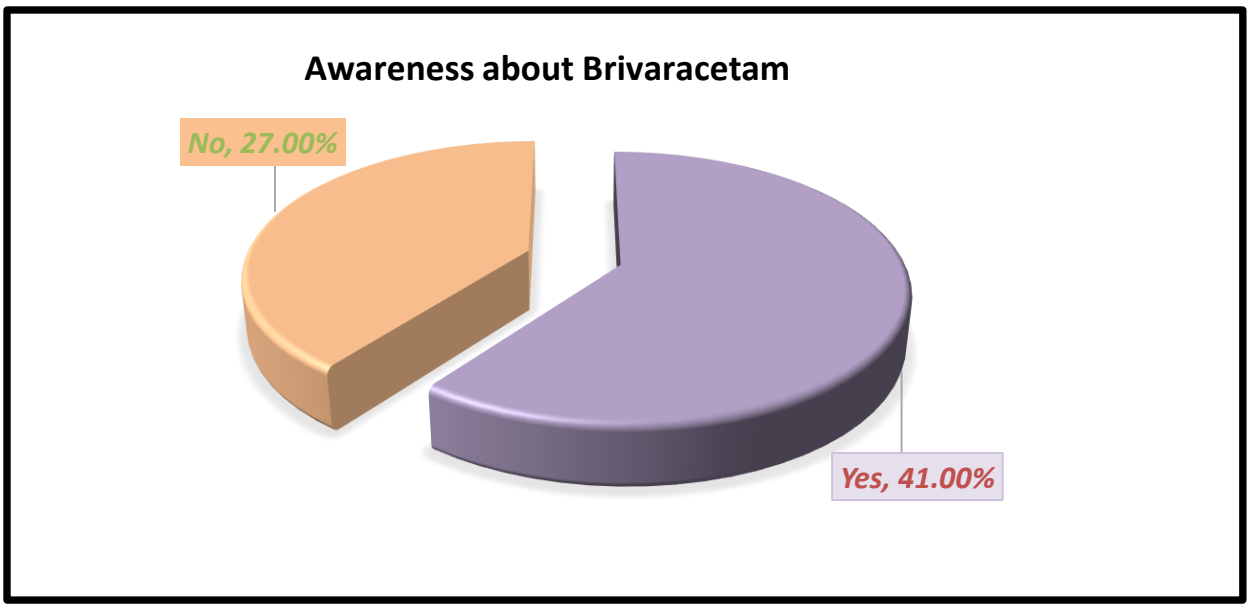


Figure 5-Shows the how much Neurologist aware about Brivaracetam.

Interpretation –

It was found that 41% of neurologists aware about the UCB new launch product brivaracetam while 27% of neurologists were not having idea about new launch anti-epileptic drug.

6. Which patients would you put on Brivaracetam?

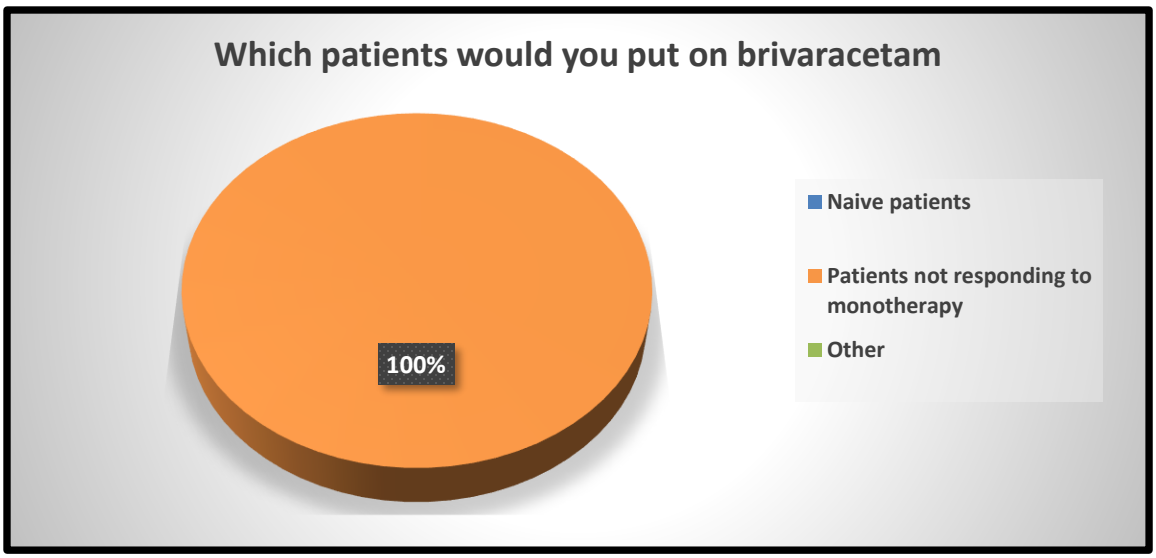


Figure 6-Shows the how much percent of patients would Neurologist like to put on Brivaracetam.

Interpretation –

From above interpretation, only 41% of neurologist aware about Brivaracetam, out of them 100% of neurologists said they would like to put on Brivaracetam, the patients which do not responding to monotherapy, reason being it is also an add-on therapy drug & more potent from levetiracetam & lacosomide with very less side effects,it will be use as alternative choice of add-on in future for partial onset seizures.

Findings based on opinions-

Personal appointments were taken to do neurologists survey in Mumbai & Delhi for "Perception mapping of customer insights on choice of Anti-Epileptic drug & Awareness about Brivaracetam". 06 questions were introduced to them. Responses recorded directly on questionnaire. Motive behind this survey is to find neurologist's choice of monotherapy, most frequently used add-on in partial onset seizure & awareness about Brivaracetam.

Following opinions of neurologist were observed:

- In partial onset seizures, neurologist's usual choice of monotherapy was found that -
    1. Carbamazepine
    2. Sodium valproate.
- Mostly 20-40% of patients in their practice do not respond to monotherapy.
- According to neurologist, in partial onset seizure frequently used add-on were found that -
    1. Levetiracetam
    2. Lacosomide
    3. Clobazam
- The neurologist's most important criteria for ideal first add-on in POS were found that –
    1. Levetiracetam – Faster onset action, less drug to drug interaction & high safety & tolerability profile
    2. Lacosomide – High Seizure freedom rates & can safely give in comorbid conditions.
    3. Clobazam - Faster onset action & High Seizure freedom rates.
- In Mumbai & Delhi, total 70 neurologists were surveyed, among them approximately 41% of neurologists is aware about recently new launch Anti-epileptic drug i.e. Brivaracetam.
- A significant difference was observed in private & government hospitals; in private hospitals all anti-epileptics are being prescribed whereas in government hospitals main focus on carbamazepine & sodium valproate as it is economical & has least side effect.
- Prescribing anti-epileptics also depends upon economic status of the patients.

Limitations –

- Sample size could have been increased in both cities i.e. Mumbai & Delhi to get more accurate results.
- Time duration of the survey did not allow to collect more data.
- The respondents were very busy & could not afford more time to answer.

Suggestions –

- The challenges will be the crowded marketplace, which currently comprises more than 20 antiepileptic drugs (AEDs), with individual drugs struggling to distinguish themselves, particularly in terms of efficacy, likewise Brivaracetam could be future market driver as it is having more potency & less side effects.
- In the future, physicians would like to see distinct new classes of AEDs that target different mechanisms, rather than more of the same drugs that currently dominate the market.
- The drivers for market growth will include the introduction of the newer drugs into the Asian market, particularly in Japan, India and China will also contribute to market growth as their populations obtain increasing access to epilepsy pharmacotherapy.
- The greatest unmet need in epilepsy remains the inadequate control of seizures that occurs in 20 to 30 percent of drug-treated epilepsy patients, translating into a significant market opportunity.
- Lacosomide gaining good market share even after the patent expiration, company wish to focus on maintain its major-market sales-leader position in coming years.
- As India is developing country, with a large population not being financially strong, carbamazepine & sodium valporate is choice of monotherapy because of cost-effectiveness, in majority of the hospitals espiscially in government hospitals even in some government hospitals there was no availability of levetiracetam & lacosomide at their drug stores.

Conclusion-

From the study it was concluded that, most of newer AED have been tested as add-on therapy in drug resistant epilepsy and are not superior to the first generation AEDs in efficacy. The main advantage of some of the newer agents was their better tolerability and pharmacokinetic profiles compared to the earlier AED. Other than Oxcarbazepine for partial epilepsy, there is no evidence for the use of the newer AED as monotherapy in new-onset epilepsy. AEDs can enhance quality of life and can help to reduce the number of seizures. Although all medications have some side effects, the choice of which drug and which side effects can be tolerated depends on each individual. AED therapy is the primary treatment for most patients with epilepsy. Early diagnosis and treatment of seizure disorders with a single appropriate therapeutic agent offer the best prospect of achieving prolonged seizure-free periods with the lowest risk of toxicity. The overall goals are to prevent seizures entirely with a minimum of adverse events and to provide a dosage schedule that is easy to follow.

Generally, first line AED's used for the monotherapy while newer AED's used as a add-on therapy. Monotherapy is the first step to try for all patients with newly diagnosed epilepsy. Following an ineffective or intolerable initial monotherapy, the next step is to add or switch to another AED. Evidence has indicated that add-on therapy might be more effective when started immediately after the first drug failure rather than after a second drug has also failed.

After failing to achieve sustained seizure freedom with two tolerated, appropriately chosen and administered AEDs (regardless of monotherapy or multitherapy) in a patient, the patient could be classified as having drug-resistant epilepsy. When add-on therapy is warranted (for those who either failed the first monotherapy or have drug-resistant epilepsy), seizure characteristics, drug and patient factors become an important consideration when implementing the management strategies. Selection of an AED is usually made based on the seizure type, spectrum of activity, tolerability, drug interaction, and patient's personal circumstances. Similar to all the other newer generations of AEDs, BRV has been investigated as an adjunctive therapy for adult patients with uncontrolled partial-onset epilepsies.

Annexure -

“ QUESTIONNAIRE”

NAME OF THE DOCTOR:-

PLACE:-

CONTACT DETAILS: -

YEARS OF PRACTICE:-

We seek your valuable feedback based on your clinical experience.

1.] In partial onset seizures, which are your usual choice of monotherapy (rate them on 1 to 5).

- ☐ **Carbamazepine**
- ☐ **Levetiracetam**
- ☐ **Lacosamide**
- ☐ **Sodium valproate**
- ☐ **Any other…….**

2.] How many percent of patients in your practice do not respond to Monotherapy in POS?

_____

3.] The most frequently used add on in POS is?

- ☐ **Carbamazepine**
- ☐ **Levetiracetam**
- ☐ **Lacosamide**
- ☐ **Sodium valproate**

☐ **Clobazam**

☐ **Any other_____**

4.] The most important criteria for ideal first add on in POS for you?

	Levetiracetam	Topiramate	Lacosamide	Clobazam	Carbamazepine
Faster onset of action					
Seizure freedom rates					
Drug to drug interactions					
Can be safely given in comorbid conditions					
Safety and tolerability profile					
Other (Specify)					

5.] Are you aware about Brivaracetam?

☐ **Yes**

☐ **No**

6.] Which patients would you put on Brivaracetam?

☐ **Naïve patients**

☐ **Patients not responding to Monotherapy**

☐ **Which patient group? _____**

BRIVARACETAM SHOW CARD

BRIVARACETAM

Brivaracetam is the novel anti-epileptic drug, Europe & US FDA approved as adjunctive in partial onset seizure.

MECHANISM OF ACTION: - It has a high affinity synaptic vesicle protein 2A (SV2A) ligand that exceeds the binding potential of Levetiracetam(LEV) by 10-30 fold & 10 times more potent for the prevention of certain type of seizure than Levetiracetam.

CLINICAL DATA:-It has a vast amount of clinical data for adult's partial onset seizure.

DOSAGE & TITRATION: - Simple dosing with no up-titration in adult epilepsy patients with partial onset seizure.

SAFETY: - It is effective & well tolerated in patients with Partial onset seizure(POS) with common side effect of drowsiness, dizziness & nausea.

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