Summer Training at
MSN Laboratoreis Pvt. Ltd., Hederabad
(April 3 to June 2, 2017)

Post Marketing Assessment of Lurasidone and Levitiracetam

By
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Under the guidance of
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MBA Pharmaceutical Management
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INSTITUTE OF HEALTH
MANAGEMENT RESEARCH
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IIHMR UNIVERSITY

CERTIFICATE

This is to certify that **Mr. Amulya Sharma has** undergone summer training in **M.S.N Laboratories at Varanasi** from **10th April to 10th June, 2017**.

The candidate himself completed the project assign to him during summer training. His approach to the project was sincere and proactive. This summer training is in partial fulfillment of the course requirement recommended for the award of MBA in Pharmaceutical Management

I wish him success in all his future endeavors.

Col. (Dr.) Ashok Kaushik
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July 17, 2017

TO WHOMSOEVER IT MAY CONCERN

This is to certify that **Mr Amulya Sharma**, s/o Sushil Kumar Sharma bearing Registration No: 0061 from IIHMR University, Jaipur has successfully completed his project work in our Formulation Marketing Department on **"Post Marketing Assessment of Lurasidone and Levetiracetam"** at MSN Laboratories Pvt. Ltd under the guidance of **Mr.Girish Misra - Sales Manager, CNS Division** from 6th April, 2017 to 30th June, 2017.

During Project work **Mr Amulya Sharma** Performance was found satisfactory.

for MSN Laboratories Pvt. Ltd

P Narsimha Rao
Senior Vice President - Group HR

Acknowledgement

The successful completion of the project would be incomplete without the mention of the people who made it possible

I would like to pay sincere thanks and respect to my Institute Mentor Dr. Saurabh Banerjee, Lecturer, Indian Institute of Health Management Research and my Organization Mentor Mr. Girish Mishra, Area Manager, North, MSN Laboratories for their constant support and advice, encouragement & every possible help in the overall preparation of this report.

I would like to take the opportunity and chance to thank a large number of individuals for their help and encouragement to make the internship successful. I am grateful to Mr. to constant guidance, support & valuable suggestions during the time of Practical Orientation.

Amulya Sharma

MBA-PM 08

IIHMR Jaipur

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Section 1- INTRODUCTION

1.1 About Organization

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With a committed and experienced group of more than 3500, the hierarchical condition at MSN Labs, established in 2003, is an exploration based pharmaceutical organization in India. It is one of the main makers of Dynamic Pharmaceutical Fixings and Completed Measurements in India. The organization is headquartered in Hyderabad, Telangana. Its nearness is set apart in 65 nations crosswise over globe covering the US, Europe, Latin America, Center East, Asia Pacific, Africa and CIS markets. also, Its Item Bushel Offers more than 200 APIs &120 Plans Covering 35 Noteworthy Treatments. Bragging a various item portfolio, with different items in the market and in the pipeline, MSN has 8 Programming interfaces (counting Oncology) and 3 completed measurement offices (counting one for oncology) and a coordinated Research and development Community for Contract Exploration and Assembling Administrations (Packs) situated in Hyderabad.

Advancement and speed frame the center of Business methodology of the Firm. professional dynamic showcasing, strong IP technique, imaginative Research and development mastery, dynamic SCM, understanding driven IT and world class capacities are our fixings to achievement

coordinates various trains and capacities by comprehensive correspondence of objectives and destinations through innovation and estimations of Uprightness, Crea Ptive energy and Advancement

It has developed from USD 0 to USD 250 million in only 12 years.

With a remarkable workforce, bleeding edge science, cutting edge innovation base and learning concentrated activities, MSN Labs chips away at creating inventive answers for tomorrow`s human services issues.

Levilex(Levetiracetam) is firm’s famous brand for Epilepsy &**Lurata(Lurasidone)** in Schizophrenia and Bipolar Depression.

1.2 BACKGROUND OBJECTIVE AND RATIONALE OF THE STUDY-

ANTI PSYCHOTICS

The therapeutic efficacy of the antipsychotic drugs is mostly related to their ability to bind & block to the dopaminergic D2 receptors in the mesolimbic system. At least 5 different subtypes of dopamine receptors have been described. They are distributed in the limbic region, the frontal cortex, the basal ganglia, the midbrain and the medulla. In addition to the dopaminergic d2 receptor blockade, some (atyoiical) antipsychotics like risperidone and clozapine also block 5HT receptors in the frontal cortex and the striatal system, which helps to lessen EP reactions and is related to their usefulness in improving negative systems. Atypical Antipsychotic has a wide receptor affinity and also block alpha 2 adrenergic receptors. Thus, the pharmacological action profile of these drugs and their adverse reactions can be explained to some extent on the basis of their receptor affinity.

MOLECULE PERSPECTIVE

Lurasidone is a Dopaminergic and Serotonergic receptor antagonist introduced in US market in the year 2011 under the brand name Latuda by "Sunovion Pharmaceuticals Ltd". Latuda got USFDA approval on October 28th 2011 for the treatment of Patients with Schizophrenia. In May 2013, USFDA approved Latuda for treatment of patients with bipolar depression

Lurasidone belongs to the cklass of Atypical Antipsychotics, Lurasidone is generic name, International Brand Name is Latuda.Lurasidone the novel anti-psychotic has potent binding affinities for 5-HT_{2A}, 5-HT_7, 5-HT_{1A}, D_2, and noradrenaline α_{2C} receptors.It is a Effective treatment choice for patients with Schizophrenia and has minimal extrapyramidal, cardiovascular, and metabolic complications.

BENEFITS OF LURASIDONE OVER OTHER MOLECULES:

- Existing molecules have certain limitations i.e. less efficacy or more side effects
- Lurata comes with the package of strong efficacy and better tolerability

ANTI- EPILECTICS

Antiepilectic drugs also known as Anticonvulsanrts,are a diverse group of pharmacologicalagents used in treatment of epilepsy(epileptic seizure)

Types of Antiepileptics

- Sodium channel blockers (Carbamazepine, Phenytoin, Fosphenytoin, Oxcarbazepine, Lamotrigine, Lacosamide)
- Calcium channel blockers (Sodium Valproate, Pregabalin and Gabapentin)
- GABA enhancer
- Glutamate blockers (Felbamate, Topiramate)
- GABA Receptor Agonists (Clobazam, Clonazepam, Phenobarbital, Primidone)
- AEDs with Other Mechanisms of Action

  (SV2A-binding agents (Levetiracetam)

MOLECULE PERSPECTIVE

LEVETIRACETAM

(belongs to the Class of AEDs)

Mechanism of Action-Synaptic vesicle release modulation

Characteristics of Levetiracetam:

- GTC, Myoclonic, Partial seizure, JME, Idiopathic generalized epilepsy, Early and late onset occipital seizure, Benign epilepsy
- No Drug-Drug interaction
- It can be use in Pregnancy
- Linear kinetics, easy for titration
- It can be use in co-medication

Side Effects

- Produces Sedation, fatigue, incoordination and Psychosis
- Produces Leucopenia, Anaemia

INDICATIONS

First line therapy and also as Adjunctive therapy in the treatment of:

- Partial onset seizures
- Myoclonic seizures
- Primary generalized tonic-clonic seizures

1.3 WHY STUDY IS IMPORTANT?

- The study demonstrates Patient Response and Compatibility to the Lurasidone & Levetiracetam and to report any rare adverse drug event related to these.
- This Study identifies the value of brand Levetiracetam and Lurasidone.
- This Study identifies the barriers in marketing of brand.
- This study examines the Advantages & Disadvantages associated with using of the brand (Levetiracetam & Lurasidone).

1.4 DISEASE PROFILE

EPILEPSY

Epilepsy is a collective term for a group of chronic seizure disorder having in common, sudden and transient episodes of loss or disturbance of consciousness, usually, but not always with a characteristic body movement, and sometimes with autonomic hyperactivity**.**

Epilectic Seizures ar classified into

1. Primarrily generalised seizure

Tonic clonic seizure

are generalized from their earliest manifestations a nd are accompanied by a generalised abnormality n the EEG. They are chahcterised by sudden loss of consciousness without any warning followed by generalized tonic convulsive movments. This is followed by a period of headache, drowsiness, confusion and sleep.

1. Atonic seizure

2. Clonic Seizure

3. Tonic Seizure.

4. Myoclonic Seizure.

2. Partial Seizure are of two types:

(a)Simple Partial Seizure

(b)Complex Partial Seizure

3. Secondarily generalised seizure

Status Epilepticus-

Prolonged seizures or repetitive seizures without recovery of consciousness between attacks comprises Status Epilepticus. When tonic clonic seizures go into status epilepticus, the situation can be life threateninig and is declared a medical emergency.

Pathophyisiology of epilepsy involves two natural movements1. Hyperexcitability 2. Hypersynchrony. hyperexcitability is the abnormal responsiveness of the neurons to an excitatory input. Leading to multiple discharges. Chronic hyperexcitability can result from number of mechanisms. Hypesynchrony refers to the recruitment of a large number of nearby neuons to an abnormally firing mode**.**

Thus Epilepsy is a network phenomenon involving participation of many neurons firing simultaneouslyThe characteristic pathophysiologic event in a sizure is believed to be paraoxysymal depolarisation shift9PDS).of neuronal membrane potential and associated burst change.

SCHIZOPHRENIA

Schizophrenia is a mental disorder characterized by persistent disturbance in the perception and evaluation of reality, leading to characteristic changes in the perceptions, thinking and behaviour.

The word schizophrenia was coined from a Greek word meaning split mind. To describe a mental syndrome where a n individual is dominated by one set of ideas or a complex to exclusion of others. Thus the harmonious working of the mind is split, with one portion seizing control of the rest**.** The schizophrenic patient, therefore, lives in his own world, dissociated from reality. He is a victim of illusions, hallucinations, and delusions. And believes that only his behaviour and actions are rational.

SYMPTOMS ASSOCIATED WITH SCHIZOPHRENIA

Positive Symptoms

- Hallucinations
- Disorganized speech &behavior

Negative Symptoms

- Blunted affect

- Emotional withdrawal
- Poor rapport
- Passivity

Cognitive Symptoms

Difficulties with***:***

- Attention
- Problem solving
- Working memory
- Speed of processing

Affective Symptoms

- Depressed mood
- Anxious mood
- Guilt
- Tension
- Irritability
- Worry

Aggressive Symptoms

- Verbal or physical abuse
- Self-injurious behaviour
- Destructive behaviour (arson, property damage)

NEUROBILOGY OF THE DISEASE

- *The Dopamine Theory or Hypothesis:*
    - The excess of dopamine level in the brain could result schizophrenia.
- *Role of Dopamine in the Brain***:**

    IQ / Cognition / Alertness

BIPOLAR DEPRESSION

Bipolar depression is the bipolar disorder. It causes depression period and elevated mood period. It consists of two Phases Manic and Depressive Phase. They feel happiness and sadness at the same time. It is characterized by difficulty in concentrating, experiencing suicidal thoughts, likely to experience Obsessive Compulsive Disorder.

1.5 RATIONALE

This study will help to reduce the serious undesired effects on Epilepsy and Schizophrenia patients due to Adverse Drug reactions of Lurasidone & Levetiracetam.

1.6 RESEARCH QUESTION-

- What is the market reach of Lurasidone & Levetiracetam in Varanasi area?
- What are the possible adverse effects related with the use of Lurasidone & Levetiracetam in general population using it?

1.7 OBJECTIVE

- To identify the number of medical practitioners prescribing the lurasidone & levetiracetam
- To confirm the safety of lurasidone & levetiracetam after it is used in general population by patients of bipolar depression and schizophrenia
- To develop information about drug effects under customary condition of use of lurasidone & levetiracetam.

Section 2- MODE OF DATA COLLECTION

2.1 METHODOLOGY-

STUDY DESIGN: This is a Cross sectional type of Study. The Location of Study was Chosen as Varanasi Area. The Study was conducted in the community among 54 Doctors. So, sample Size was 54.This Study was also a type of Purposive Sampling as it was based on characteristics of the population and the objective of the Study.

ANALYSIS PLAN: This was a Quantitative & Analytical Study.

The Study was done on the Basis of Primary Data and generated by Doctor and Chemist Survey.

DATA COLLECTION METHOD: A specially designed Questionnaire was prepared as data collection tool.

The response rate was low to the Questions asked on the spot.

DATA TYPE: Nominal

PROBLEMS OCCURRED IN GATHERING DATA:

- Improper Attention
- Lack of Adequate Time
- Some Doctors misinterpreted Survey as a Promotional Activity of the Company

2.2 MATERIALS USED-

The data was collected through Structured Questionnaire. A Questionnaire of 10 questions was developed for post marketing survey of Luasidone & Levetiracetam.

QUESTIONNAIRE FOR LEVETIRACETAM

1. In the management of Epilepsy which of these molecules will be on top of your mind

A. Levetiracetam B. Oxcarbazepine C. Valproate D. Others

2. Preferred indication for prescribing Levetiracetam to the patients

A. Partial Onset Seizures B. Juvenile Myoclonic Seizures

C. Generalised Seizures D. All the above

3. What's the length of Levetiracetam prescription for your patients

A. Upto 3 years B. No timelines C. Based on the patient's response

4. My Choice of prescrbing Levetiracetam is as

A. Monotherapy B. Adjuvant therapy C. Both Choice A / B based on the need

5. Have you come across cognition disturbance with the patients who are on Levetiracetam monotherapy?

A. No B. Yes C. Can't comment

6. How frequently you shift the brands of Levetiracetam for your patients?

A. Yes, if only quality issues are there B. Yes, if only availability issues are there

C. Both A and B

7. Will you continue to prescribe the brand of Levetiracetam if that brand is acquistioned by some other company?

A. Yes. My epileptic patients are responding well to that concerned brand because of its

quality. So will continue prescribing.

B. Will think over it and take a decision.

8. Will price be a concern for you to choose the brand of Levetiracetam?

A. No B. Yes

9. In your opinion do you feel Levetiracetam will remain as the most preferred molecule to treat Epilepsy?

A. Yes B. Let's wait and watch for the new molecules

10. Would you appreciate any novel formulations of Levetiracetam?

A. Yes B. No

QUESTIONNAIRE FOR LURASIDONE

1. How is your experience with the latest Anti-psychotic drug Lurasidone for managing Schizophrenia in the last 8 months

a) Excellent b) Good c) Moderate d) Poor

2. Your preference of the drug Lurasidone is widely to manage

a) Schizophrenia b) Bipolar Depression

c) Schizophrenia & Bipolar Depression d) Not tried yet

3. Your preferred prescribing dose of Lurasidone to manage Schizophrenia

a) Above 80 mg b) 40 – 80 mg c) 40 mg d) 80 mg

4. Your preferred prescribing dose of Lurasidone to manage bipolar depression

a) Above 80 mg b) 40 – 80 mg c) 40 mg d) 20 mg

5. Your choice of prescribing Lurasidone to manage Schizophrenia

a) Monotherapy b) Combination with other anti-psychotics

6. Your choice of prescribing Lurasidone to manage Bipolar depression

a) Monotherapy b) Combination with other drugs

7. The concerns that limits your prescriptions to recommend Lurasidone

a) Dose Titration b) Side-effects c) Efficacy d) None

8. How is the Response rate of your Schizophrenia patients to Lurasidone?

a) Excellent b) Moderate c) Poor

9. Maximum number of scientific articles strongly endorses the usage of Lurasidone in bipolar depression. Your opinion on the same.

a) Agree b) Strongly Agree c) Disagree

10. Your take on the molecule Lurasidone

a) Lurasidone has a role to play b) Moderate Scope c) Cannot comment.

Section 3- DATA COMPILATION, RESULTS AND DISCUSSIONS-

RESULTS

Levetiracetam

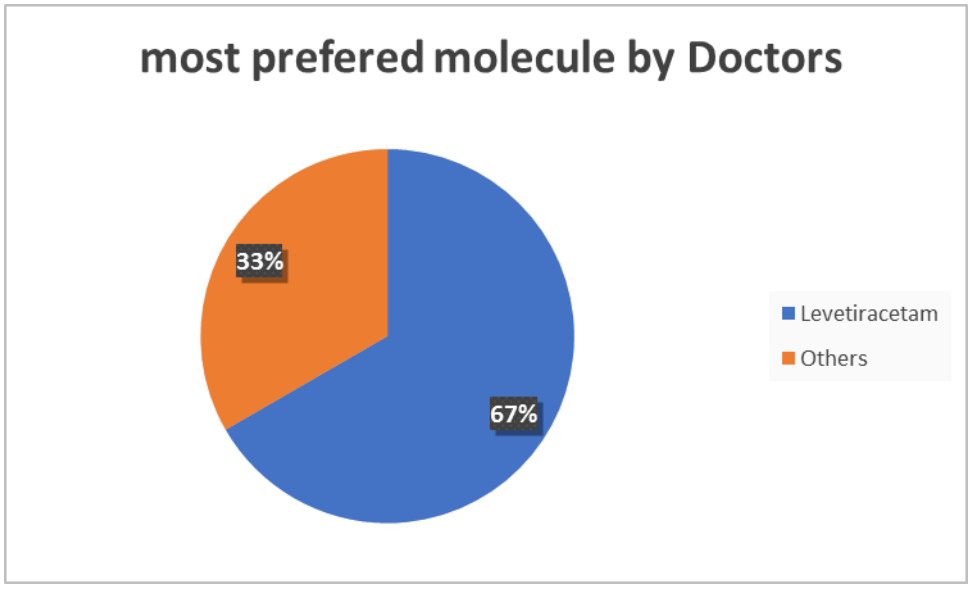
- In the Case of Levetiracetam, Many Doctors said that they don't prescribe it.
- Few doctors also refused to say anything or share anything about medicine as they objected that patient response to any drug is a private Information and shouldn't be shared.
- The doctors who said they prescribe Levetiracetam were quite satisfied by the product.
- Cognition disturbance was noted in some patients of Epilepsy using Levetiracetam.
- Patient Response to Levetiracetam was Moderate.
- Price is not a Concern for prescribing the Levetiracetam.

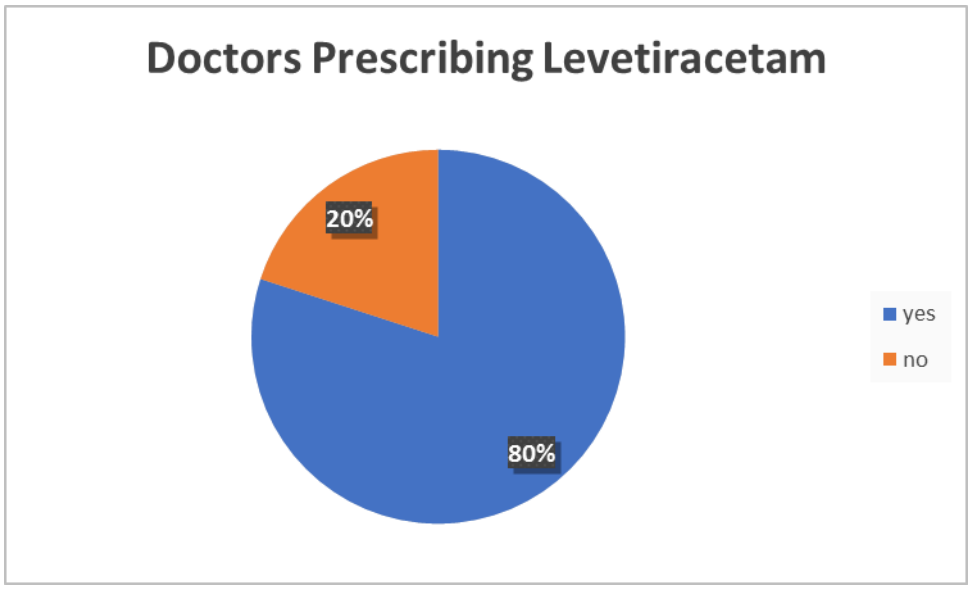
Lurasidone

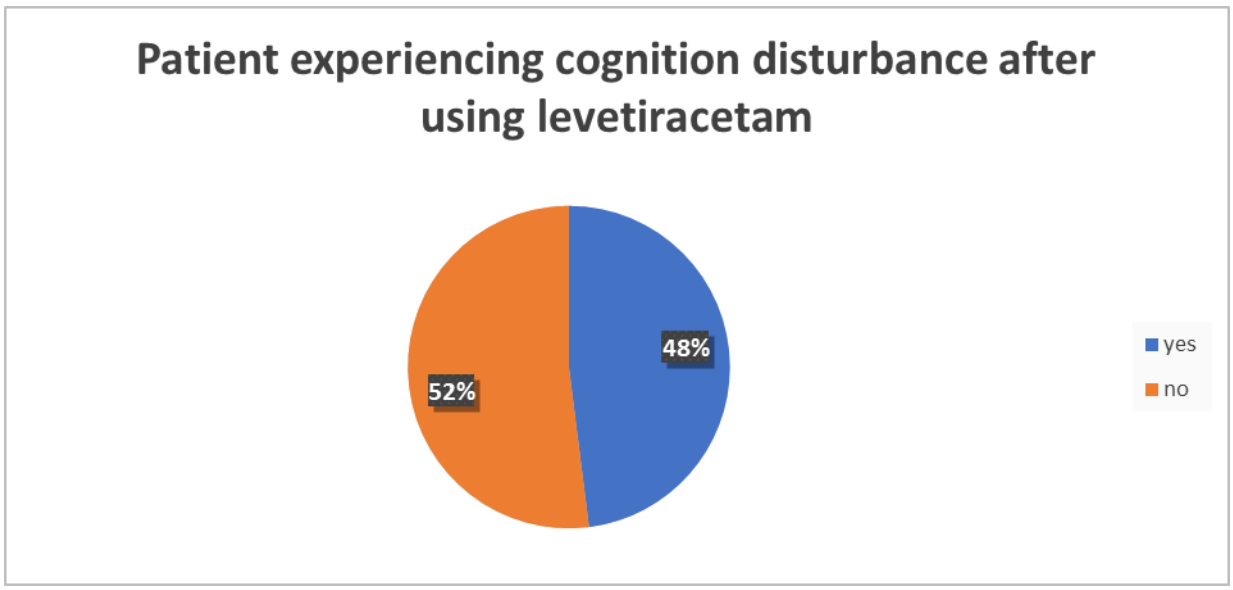
- While in the Case of Lurasidone, half of the Psychiatrists said that they prescribe it while rest few denied.
- Some Psychiatrists said that they have just started to prescribe Lurasidone and they can't give feedback.
- Patients were most compatible to Above 80 mg dosage in Schizophrenia and 40-80mg dosage in Bipolar Depression.
- It is mostly prescribed by Psychiatrists as Monotherapy.
- Efficacay is a issue in prescribing the Lurasidone by Psychiatrists.

ANALYSIS

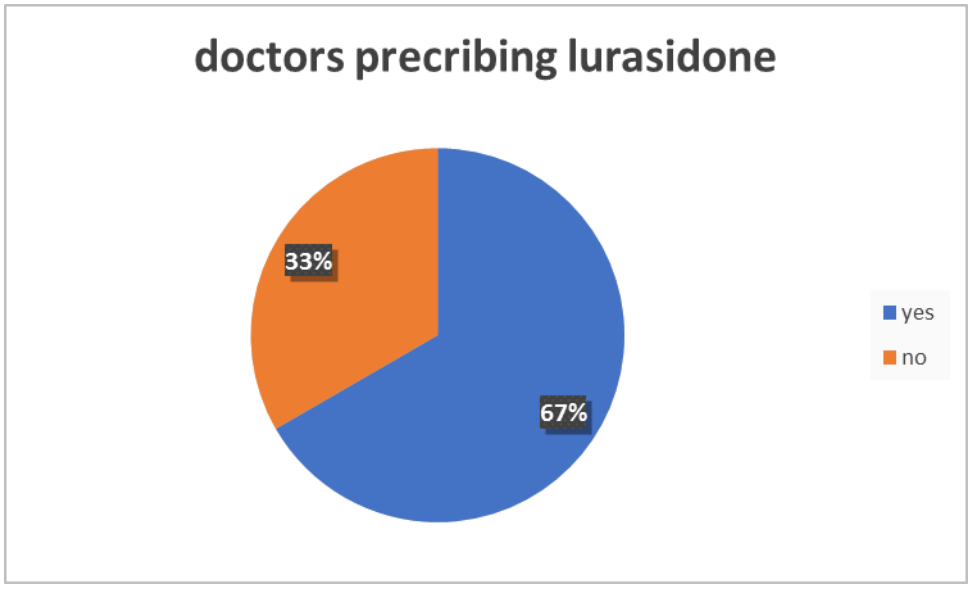
Prescription pattern of Levetiracetam among Neurophysicians

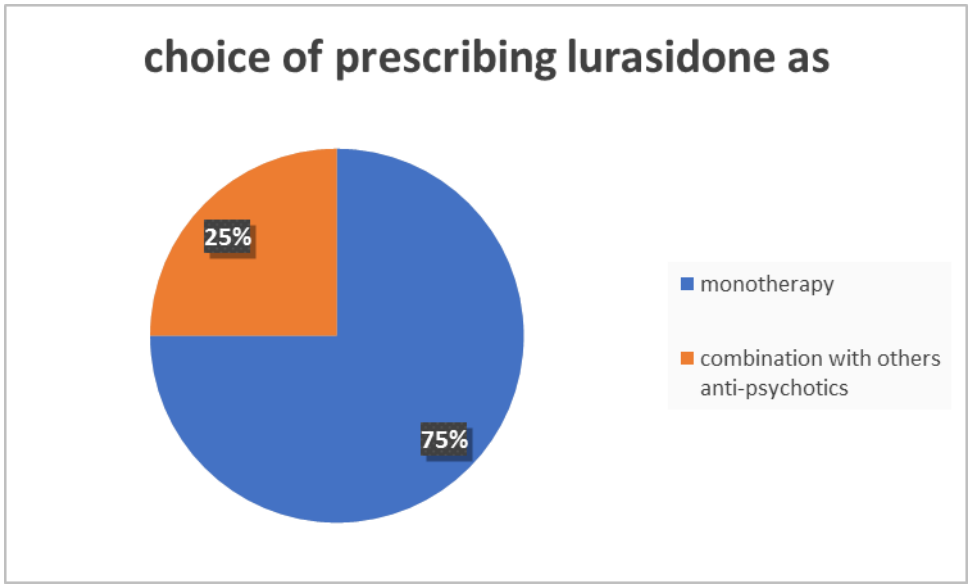


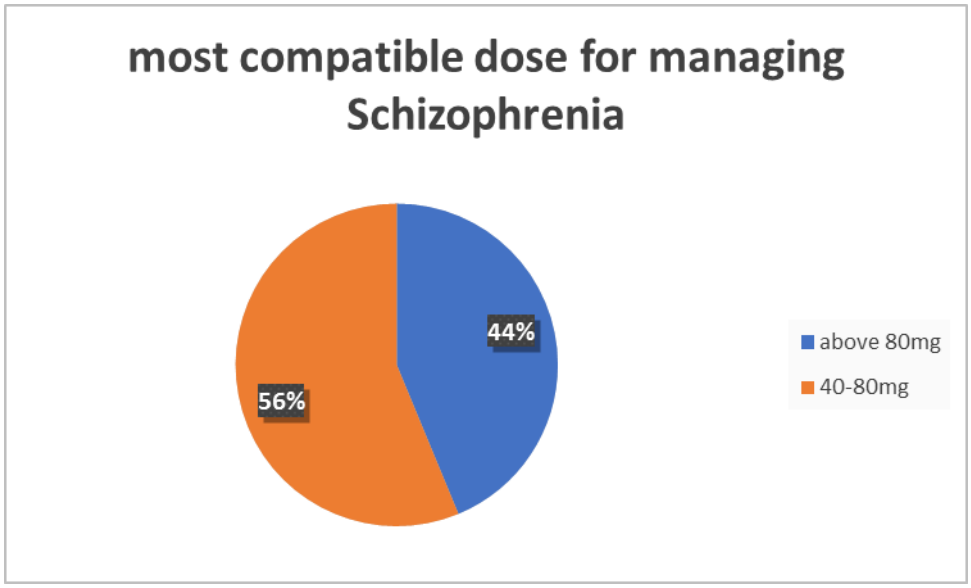




Prescription Pattern of Lurasidone among Psychiatrists




choice of prescribing lurasidone as
25%
75%
monotherapy
combination with others anti-psychotics


most compatible dose for managing Schizophrenia
44%
56%
above 80mg
40-80mg

CONCLUSIONS-

This Post Marketing assessment indicates the Overall Market for the products (anti-psychotic and Anti epilectic) in Varanasi area.

Following points can be Concluded from the Study for Lurasidone:

- Lurasidone is not prescribed by experienced and established Doctors.
- Lurasidone Market is developing and emerging one.
- Lurasidone is way behind in proving its effect among patients of Schizophrenia and Bipolar Depression.

Following points can be concluded from the Study for Levetiracetam:

- Levetiracetam has Satisfactory Patient Response.
- Levetiracetam Market is good but any Novel and Innovative molecule can replace it in Future.

RECOMMENDATIONS-

- Better Marketing Strategies to be implemented.
- Increase Brand awareness of Levetiracetam & Lurasidone.
- Better Advertising needed.
- Organizing Free Camps.
- Free Sample Distribution in Poor Patients.

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