NEW ANTIPSYCHOTICS, ANTISEIZURE AND ANTIDEPRESSANT MEDICATIONS 2015-PRESENT

Nanette R Wrobel, RPh
Director of Education/Clinical Director
Pharmacy Alternatives

OBJECTIVES

- Review new medications approved in past 30 months.
- Identify important side-effects of new medications.
- Recognize appropriate use of medications including dosaging, administration, and indications.

WHY?

- New medications are constantly being approved or having new indications are approved by the FDA.
- Need for improved antipsychotics, as current medications have room for improvement., either with their indication, mechanism of action, or side effect and drug interaction profile.

NEW MEDICATIONS AND INDICATIONS: 2015[1]

- Latuda (lurasidone)
- Aristada (Aripiprazole Lauroxil) Extended-Release Injectable
- Rexulti (Brexpiprazole)
- Vraylar (Cariprazine)

NEW MEDICATIONS AND INDICATIONS: 2016[2]

- Briviact (Brivaracetam)
- Carnexiv (Carbamazepine)
- Nuplazid (Pimavanserin)

NEW MEDICATIONS AND INDICATIONS: 2017[3]

- As of March 10th, 2017 there have been no new FDA approvals for either new medications nor new indications for anticonvulsants, antipsychotics, and/or antidepressants.
- One medication, Retigabine (Potiga), will no longer be available due to lack of usage. SE: abnormalities of the retina. Adjunctive treatment of partial onset seizures.

2015 FDA APPROVALS

REXULTI (BREXIPIPRAZOLE)[4,5]

- Approved by the FDA in July 2015
- Approved for treatment of schizophrenia and adjunct treatment of Depression
- Atypical antipsychotic
- Mechanism of Action is currently unknown; D2 partial agonist
- Why developed?
  - Current medications for treating depression and schizophrenia vary in terms of efficacy and side-effect profile leaving much to be desired in terms of finding a medication that works optimally for patients.

REXULTI (BREXIPIPRAZOLE)[4,5]

- Two major trials proved efficacy of Rexulti in treatment of Schizophrenia and as an adjunctive treatment for Major Depressive Disorder (MDD)
  - Dosing for Schizophrenia is recommended to start at 1mg once daily taken orally with or without food and to be titrated up to a max daily dose of 4mg over the course of the first 7-8 days.
  - Dosing for MDD is as an adjunct to 1st-3rd line antidepressants with a recommended starting daily dose of 0.5mg by mouth taken with or without food. Titrate on weekly intervals to recommended daily dosage of 3mg.

REXULTI (BREXIPIPRAZOLE)[4,5]

- Not indicated in Pediatric Patients
- Boxed Warning
  - Increased mortality In elderly patients with dementia-related psychosis and a potential risk in the increase of the risk of suicidal thoughts and behaviors in patients 24 years or younger with use of antipsychotic drugs
- Side-Effects:
  - Akathisia
  - Weight Gain
  - Potential Tardive Dyskinesia
  - Possible orthostatic hypotension

VRAYLAR (CARIPRAZINE)[6,7]

- Approved by the FDA in September 2015
- Approved for the treatment of Schizophrenia and Bipolar Disorder
- Atypical antipsychotic
- Mechanism of Action is currently unknown, although thought to be part of a new class of partial agonist/antagonists and stimulates D3 receptors (cognitive enhances for neuropsychaiatric conditions such as autism, schizophrenia, parkinsonism and Alzheimer's Disease
- Why developed?
  - Improved treatment of schizophrenia and bipolar disorder is constantly driving new drug research.

VRAYLAR (CARIPRAZINE)[6,7]

- Multiple studies were conducted to evaluate efficacy of Vraylar in treating Schizophrenia and manic or mixed episodes associated with Bipolar I Disorder
- Dose-related increase in adverse reactions seen in patients receiving more than 6mg/day
- Recommended dose range for treatment of Schizophrenia is 1.5mg to 6mg once daily. Start at 1.5mg, can increase to 3mg on day 2, etc.
- Recommended dose range for treatment of manic or mixed episodes associated with Bipolar I Disorder is 3mg to 6mg once daily.
- For both disease states, dose adjustments can be made in either 1.5mg or 3mg increments.

VRAYLAR (CARIPRAZINE)[6,7]

- Drug Interactions:
  - CYP 3A4 Inhibitors itraconazole, ketoconazole: reduce dose
  - CYP3A4 Inducers: rifampin, carbamazepine; concommitent use not recommended
- Boxed Warning
  - Increased mortality in elderly patients with dementia-related psychosis and a potential risk in the increase of the risk of suicidal thoughts and behaviors in patients 24 years or younger with use of antipsychotic drugs
- Side-Effects:
  - Extrapyramidal symptoms
  - Akathisia
  - Dyspepsia
  - Vomiting
  - Restlessness
  - Somnolence
  - Potential Tardive Dyskinesia
  - Possible orthostatic hypotension

LATUDA (LURASIDONE)

- Indicated for treatment of schizophrenia and acute depression of bipolar disorder
- 2nd generation andtipsychotic, antagonizes dopamine D2 receptors and seratonin 5-HT2A receptors
- Used in adults for both schizophrenia and bipolar depression Bipolar I as monotherapy and as adjunctive therapy with valproic acid and lithium and in children 13-17 yrs old for schizophrenia

LATUDA

- Boxed warnings:
  - Elderly with dementia
  - Suicidality in young adults
- Side effects:
  - Angioedema
  - CNS
  - GI
  - Monitor for blood sugar elevations, hyperlipidemia

LATUDA

- Drug interactions
- :Strong CYP3A4 inducers: rifampin, carbamazepine
- Strong CYP450 inhibitors: ketoconazole

- Dosing:
- Adults with schizophrenia: 40mg/day with food. May increase to max of 160mg/day
- Adults with Bipolar I depression: start at 20mg/day may increase to 80mg/day with food
- Children with schizophrenia: start at 40mg/day with food. Max is 80mg/day

ARISTADA (ARIPIPRAZOLE LAUROXIL)[8]

- FDA approved in October 2015
- Approved for treatment of schizophrenia
- Atypical antipsychotic supplied as a solution for Intramuscular administration.
  - Administer in either the deltoid muscle (441mg dose only) or the gluteal muscle (441mg, 662, or 882mg doses only)
- Mechanism of Action is currently unknown for Aripiprazole, however Aristada is a prodrug of Aripiprazole and is metabolized into aripiprazole while in the body.
- Why?
  - An extended-release injectable form of aripiprazole allows for higher doses spread out across larger amounts of time to the benefit of the patient.

ARISTADA (ARIPIPRAZOLE LAUROXIL)[8]

- FDA approval of Aristada stems from a 12-week trial that established efficacy of Aristada and trials with oral formulation of aripiprazole and their respective efficacy data regarding aripiprazole.
- Dosing for schizophrenia is at 441mg, 662mg, or 882mg injected monthly, or 882mg dose injected every 6 weeks.
- Aripiprazole-naïve patients should have tolerability established with oral aripiprazole prior to starting Aristada.

ARISTADA (ARIPIPRAZOLE LAUROXIL)[8]

- Boxed Warning
- Increased mortality in elderly patients with dementia-related psychosis and a potential risk in the increase of the risk of suicidal thoughts and behaviors in patients 24 years or younger with use of antipsychotic drugs
- Side-Effects:
  - Akathisia
  - Potential Tardive Dyskinesia
  - Possible orthostatic hypotension

2016 FDA APPROVALS

BRIVIACT (BRIVARACETAM)[9,14]

- Approved by the FDA in February 2016
- Approved for the treatment of partial onset seizures related to epilepsy
- Studied use alongside carbamazepine, lacosamide, lamotrigine, keppra, oxcarbazepine, phenobarbital, phenytoin, pregabalin, topiramate, valproic acid, and zonisamide
- Antiepileptic
- Mechanism of Action is currently unknown
- Class-V controlled substance
- Why develop med?
  - For patients not adequately controlled by 1-2 concomitant AED's and available in multiple formulations.

BRIVIACT (BRIVARACETAM)[9,14]

- FDA approval of Briviact stems from three major trials that evaluated the efficacy of Briviact.
- Available in tablet, oral solution, and IV administration formulations
  - May give tablet formulation with or without food and are to be swallowed with liquid.
  - Injection should be administered intravenously over 2-15 minutes.
  - May further dilute or mix with 0.9% NS, Lactated Ringer's, or D5W injections.
- Recommended starting dose is 50mg twice daily (100mg daily).
- May adjust dosage to as low as 25mg twice daily (50mg daily) or 100mg twice daily (200mg daily).

BRIVIACT (BRIVARACETAM)[9,14]

- Warning
  - May increase the risk of suicidal behavior and/or suicidal ideation
- Side-Effects:
  - Somnolence/sedation
  - Dizziness
  - Fatigue
  - Nausea/vomiting
  - Euphoria
  - Infusion site pain
  - Feelings of "drunkenness"

NUPLAZID (PIMAVANSERIN)[10,11,12]

- FDA approved in April 2016 for the indication of hallucinations and delusions associated with Parkinson's disease.
- Atypical antipsychotic
- Mechanism of Action is currently unknown.
- Why developed?
  - Reduces symptoms of hallucinations and delusions without impacting motor functions like other therapy options.

NUPLAZID (PIMAVANSERIN)[10,11,12]

- Both indications approved by the FDA were supported by a study that showed benefit of Nuplazid in long-term reduction of frequency and/or severity of hallucinations and delusions in patients with Parkinson's Disease psychosis.
- Recommended dosing is 34mg per day. Take two 17mg tablets once day.
  - No dose titration is advised at this time.

NUPLAZID (PIMAVANSERIN)[10,11,12]

- Boxed warning
  - Increased mortality in elderly patients with dementia-related psychosis.
- Side-Effects:
  - QT interval prolongation
  - Peripheral edema
  - Nausea
  - Confused state
  - Hallucinations

CARNEXIV (CARBAMAZEPINE)[13]

- Approved by the FDA in October 2016
- Approved for the treatment of seizures
- Antiepileptic
- Mechanism of Action is Carnexiv is a sodium channel blocker.
- Why developed?
  - Replacement therapy for patients with partial seizures with complex symptomatology, generalized clonic-tonic seizures, mixed seizure patterns, or other partial or generalized seizures who are currently taking oral carbamazepine formulations during times when oral administration is temporarily not feasible.

CARNEXIV (CARBAMAZEPINE)[13]

- FDA approval of Carnexiv was based on bioavailability studies that compared oral carbamazepine to Carnexiv and discovered comparable dosing.
- Normal dose of Carnexiv is 70% the total daily dose of carbamazepine divided into four equal infusions separated by 6 hours, diluted in 100mL of diluent, infused over 30 minutes, and not used for periods of time longer than seven days.

CARNEXIV (CARBAMAZEPINE)[13]

- Boxed warning
  - Toxic Epidermal Necrolysis (TEN) and Stevens-Johnson syndrome (SJS) have been reported following administration of Carnexiv. Following the use of Carnexiv, there is also a risk of aplastic anemia and agranulocytosis.
- Side-Effects:
  - Somnolence
  - Dizziness
  - Blurred vision
  - Diplopia
  - Headache
  - Infusion-site pain

2017 FDA APPROVALS

2017 DRUG APPROVALS

- As of this moment, no new antidepressant, anticonvulsant, or antipsychotic drugs approved in 2017
- This may very well change as the year moves forward!

- New things on the horizon:
- New Indication of Aptiom

- To obtain a certificate of participation:
  - Email Kathy Brown, RN, CDDN at kathybrown@palrx.com
- To sign up directly for more webinars:
  - Email Nanette Wrobel, RPh at Nwrobel@palrx.com
- To find out more about our pharmacy services in your area:
  - Email Nanette at Nwrobel@palrx.com or call 847-712-6578

- Please visit our new website at palrx.com!

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QUESTIONS