Neurology Drug Update

Nicole M. Quiles, PharmD, MPH
Pharmacy Director
Axium Healthcare Pharmacy

Héctor J. Hernández, PharmD, MPH, CSP
Pharmacy Director
Special Care Pharmacy Services

Learning Objectives

The target audience for this activity is healthcare professionals.

Upon completion of this activity, participants will be able to:

1. Describe the newly approved neurological drugs.
2. Outline the emerging therapies in the pipeline for neurological conditions.

Newly Approved Drugs

vigabatrin Oral Solution

Pharmacologic Category:

- Antiseizure Agent

Indication:

- Ready-to-use oral solution formulation of the approved anti-seizure medicine vigabatrin used for the treatment of infantile spasms.

Mechanisms of Action:

- The precise mechanism of vigabatrin’s anti-seizure effect is unknown, but it is believed to be the result of its action as an irreversible inhibitor of γ-aminobutyric acid transaminase (GABA-T), the enzyme responsible for the metabolism of the inhibitory neurotransmitter GABA.

vigabatrin Oral Solution

Recommended dosage:

- Initiate at a daily dosage of 50 mg/kg (25 mg/kg twice daily); increase total daily dosage every 3 days, in increments of 25 mg/kg/day to 50 mg/kg/day, up to a maximum daily dosage of 150 mg/kg (75 mg/kg twice daily).

Dosage Forms:

- Oral Solution: 100 mg/mL, 150 mL bottle

Most common adverse reactions:

- Somnolence, bronchitis, ear infection, and acute otitis media.

Warning:

- Can cause permanent bilateral concentric visual field constriction, including tunnel vision that can result in disability. In some cases, may also decrease visual acuity.

diazepam Buccal Film

Pharmacologic Category:

- Antiseizure Agent, Benzodiazepine

Indication:

- Acute treatment of intermittent, stereotypic episodes of frequent seizure activity that are distinct from a patient's usual seizure pattern in patients with epilepsy 2 to 5 years of age.

- Mechanisms of Action:
  - The exact mechanism of action for diazepam is not fully understood but is thought to involve potentiation of GABAergic neurotransmission resulting from binding at the benzodiazepine site of the GABAA receptor.

diazepam Buccal Film

Recommended dosage:

- Dose is dependent on the patient's weight. A second dose of may be administered at least 4 hours after the first, but do not exceed two doses per episode. Should not be used to treat more than one episode every five days or more than five episodes per month.

Dosage Forms:

- Buccal film: 5 mg, 7.5 mg, 10 mg, 12.5 mg, 15 mg

Most common adverse reactions:

- Somnolence and headache.

Warning:

- Concomitant use of benzodiazepines and opioids can result in severe sedation, respiratory depression, coma, and death, misuse or frequent use beyond recommendations can lead to addiction, overdose, or life-threatening withdrawal reactions.

zavegepant hydrochloride

Pharmacologic Category:

- Antimigraine Agent

Indication:

- A calcitonin gene-related peptide receptor antagonist indicated for the acute treatment of migraine with or without aura in adults.

Mechanisms of Action:

- A calcitonin gene-related peptide (CGRP) receptor antagonist.

zavegepant hydrochloride

Recommended dosage:

- 10 mg as a single spray in one nostril as needed, with a maximum of 10 mg in a 24-hour period; the safety of treating more than 8 migraines in a 30-day period has not been established.

Dosage Forms:

- Nasal spray: 10 mg

Most common adverse reactions:

- Taste disorders, nausea, nasal discomfort, and vomiting.

Warning:

- Serious hypersensitivity reactions, such as facial swelling or urticaria.

lecanemab-irmb

Pharmacologic Category:

- Anti-Amyloid Monoclonal Antibody

Indication:

- A monoclonal antibody directed against aggregated soluble and insoluble forms of amyloid beta.

Mechanisms of Action:

- Lecanemab-irmb is a humanized immunoglobulin gamma 1 (IgG1) monoclonal antibody directed against aggregated soluble and insoluble forms of amyloid beta.

lecanemab-irmb

Recommended dosage:

- 10 mg/kg via intravenous infusion over approximately one hour; once every two weeks.

Dosage Forms:

- Single Dose Vial: 500 mg/5 mL and 200 mg/2 mL

Most common adverse reactions:

- Infusion-related reactions, amyloid related imaging abnormality microhemorrhages, amyloid related imaging abnormality-edema/effusion, and headache.

Warning:

- Amyloid Related Imaging Abnormalities (ARIA; e.g., cerebral edema, hemorrhage, hemosiderin deposition; boxed warning); risk is increased in patients who are apolipoprotein E4 (APOE4) homozygotes and testing for APOE4 should be performed prior to initiating treatment.

gepirone hydrochloride

Pharmacologic Category:

- Antidepressant

- Indication:
  - An antidepressant used to treat major depressive disorder (MDD) in adults.
- Mechanisms of Action:
  - A selective partial agonist of the 5-HT1A receptor.

gepirone hydrochloride

Recommended dosage:

- 18.2 mg once a day with food at approximately the same time each day.
- Depending on clinical response and tolerability, the dosage may be increased to 36.3 mg once a day on Day 4; dosage may be further titrated to 54.5 mg once a day on Day 7, and to 72.6 mg once a day after an additional week.
- Patients with renal impairment (creatinine clearance less than 50 mL/min), or with moderate hepatic impairment – starting dosage is 18.2 mg once a day and may be increased to 36.3 mg after 7 days.

Dosage Forms:

- Extended-release tablets: 18.2 mg, 36.3 mg, 54.5 mg, 72.6 mg

Most common adverse reactions:

- Dizziness, nausea, insomnia, abdominal pain, and dyspepsia.

- Warning:
  - Increased risk of suicidal thinking and behavior in pediatric and young adult patients.

deutetrabenazine Extended Realease

Pharmacologic Category:

- Central Monoamine-Depleting Agent

Indication:

- Tardive dyskinesia and chorea associated with Huntington disease (HD).

Mechanisms of Action:

- The precise mechanism by which deutetrabenazine exerts its effects in the treatment of tardive dyskinesia and chorea in patients with Huntington’s disease is unknown but is believed to be related to its effect as a reversible depletor of monoamines (such as dopamine, serotonin, norepinephrine, and histamine) from nerve terminals.

deutetrabenazine Extended Realease

Recommended dosage:

- 12 mg once daily, dosage may be increased at weekly intervals in increments of 6 mg per day based on reduction of chorea or tardive dyskinesia, and tolerability, up to a maximum recommended daily dosage of 48 mg.

Dosage Forms:

- Extended-release tablets: 6mg, 12mg, 24mg, 30mg, 36mg, 42mg, and 48mg

Most common adverse reactions:

- HD: somnolence, diarrhea, dry mouth, and fatigue.
- TD: nasopharyngitis and insomnia

Warning:

- Risk of depression and suicidal thoughts and behavior (suicidality) in patients with Huntington's disease.

clonidine hydrochloride Extended-Release Suspension

Pharmacologic Category:

- Alpha2-Adrenergic Agonist

Indication:

- Attention Deficit Hyperactivity Disorder (ADHD) as monotherapy or as adjunctive therapy to central nervous system (CNS) stimulant medications in pediatric patients 6 years of age and older.

Mechanisms of Action:

- Clonidine stimulates alpha2-adrenergic receptors in the brain. Clonidine is not a central nervous system stimulant. The mechanism of action of clonidine in ADHD is not known.

clonidine hydrochloride Extended-Release Suspension

Recommended dosage:

- Starting dosage is 0.1 mg of clonidine hydrochloride orally once daily at bedtime with or without food. Dosage may be increased in increments of 0.1 mg per day at weekly intervals. Maximum recommended dosage is 0.4 mg once daily at bedtime.

Dosage Forms:

- Extended-release oral suspension: 0.1mg/mL, 120 mL

Most common adverse reactions:

- Monotherapy: somnolence, fatigue, irritability, nightmare, insomnia, constipation and dry mouth.
- Adjunct Therapy: somnolence, fatigue, decreased appetite and dizziness.

Warning:

- Risk of Hypotension, bradycardia and sedation.

Emerging therapies for neurological conditions

Delpacibart etedesiran

Pharmacologic Category:

- Myotonic dystrophy type 1

Target:

- TfR1

Type:

- A Phase 3 an investigational monoclonal antibody (mAb) that binds to the transferrin receptor 1 (TfR1) conjugated with a small interfering RNA (siRNA) targeting DMPK mRNA.

ABBV-951

Pharmacologic Category:

- Parkinson's Disease

Target:

- Dopamine Receptor

Type:

- A Phase 3 drug, involves subcutaneous delivery of Levodopa/Carbidopa.

ABBV-552

Pharmacologic Category:

- Alzheimer's Disease

Target:

- SV2A

Type:

- A Phase 2 SV2A modulator which is being evaluated to target nerve terminals to enhance synaptic efficiency.
- The mechanism is being evaluated for the potential treatment of cognitive impairment and other symptoms associated with a range of neuropsychiatric and neurodegenerative disorders.

ABBV-916

Pharmacologic Category:

- Alzheimer's Disease

Target:

- AßpE3

Type:

- A Phase 2 anti-AβpE3 (N-terminal truncated, pyroglutamate-modified at amino acid position 3, amyloid beta) is a monoclonal antibody being investigated for the treatment of Alzheimer’s Disease.

MK-8189

Pharmacologic Category:

- Schizophrenia

Target:

- PDE10A

Type:

- A Phase 2 inhibitor of phosphodiesterase 10A.

xanomeline-trospium

Pharmacologic Category:

- Schizophrenia

Target:

- A dual M1/M4 muscarinic acetylcholine receptor agonist

Type:

- An investigational muscarinic antipsychotic in development for the treatment of schizophrenia and psychosis related to Alzheimer’s disease.

References

- U.S. Food and Drug Administration. "LIBERVANT (diazepam) Buccal Film, 2024." https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/217645s000lbl.pdf. (Accessed on June 19, 2024).
- U.S. Food and Drug Administration. "Prescribing Information for Exxua, 2023." https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/021164s000lbl.pdf. (Accessed on June 19, 2024).
- U.S. Food and Drug Administration. "LEQEMBI (lecanemab-irmb) Prescribing Information." https://www.leqembi.com/-/media/Files/Leqembi/Prescribing-Information.pdf?hash=fc18d22c-7a52-4f23-a664-475ec683bbaa. (Accessed on June 19, 2024).
- U.S. Food and Drug Administration. "Prescribing Information for Vigafyde, 2024." https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/217684s000lbl.pdf. (Accessed on June 19, 2024).
- U.S. Food and Drug Administration. "Prescribing Information for Libervant, 2024." https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/218623s000lbl.pdf. (Accessed on June 19, 2024).
- Pfizer Inc. "Prescribing Information for Zavzpret." https://labeling.pfizer.com/ShowLabeling.aspx?id=19471. (Accessed on June 19, 2024).
- UpToDate, Post TW (Ed), UpToDate, Waltham, MA. (Accessed on June 19, 2024).