





AHCCCS Pharmacy and Therapeutics Committee

October 15, 2024

AHCCCS
Arizona Health Care Cost Containment System

P&T Agenda

- Welcome and Introductions
- Supplemental Rebate Class Reviews
- New Drug Reviews
- Executive Session
- Public Therapeutic Class Votes
- Meeting Adjournment

Welcome and Introductions

- Suzi Berman, RPh, Pharmacy Director, AHCCCS
  - Minutes Review and Vote - P&T June 18th, 2024
  - Review
  - Vote

Magellan Class Reviews

Classes for Review: Non-Supplemental Rebate Classes

- Anticonvulsants
- Antifungals, Oral
- Antifungals, Topical
- Antimigraine Agents, Triptans
- Beta Blockers
- BPH Treatments
- Calcium Channel Blockers
- Contraceptives
- Hereditary Angioedema Treatments
- HIV/AIDS
- Leukotriene Modifiers
- Movement Disorder Agents
- Phosphate Binders
- Sedative Hypnotics
- Topical Steroids – Low, Medium, High & Very High Potency




Magellan Drug Class Reviews

Umang Patel, Pharm.D.

Anticonvulsants

Anticonvulsants

FDA-Approved Indications

Drug	Manufacturer	Seizure Disorders				Neuropathic Pain	Lennox-Gastaut Syndrome	Migraine Prophylaxis	Bipolar Disorder
		Absence	Myoclonic	Partial	Tonic-Clonic				
Barbiturates									
phenobarbital[1]	generic		X	X*	X*				
primidone (Mysoline®)[2]	generic, Bausch			X*	X*				
Hydantoins									
phenytoin ER (Dilantin®)[3]	generic, Pfizer/Viatris			X*	X*				
phenytoin ER (Phenytek®)[4]	Sun, Mylan								
Succinimides									
ethosuximide (Zarontin®)[5]	generic, Pfizer	X*							
methsuximide (Celontin®)[6]	Ani, Pfizer	X*							
Benzodiazepines									
clobazam (Onfi®)[7]	generic, Lundbeck						X*†		
clobazam film‡ (Sympazan®)[8]	Aquestive/Otter						X*†		
clonazepam (Klonopin®)[9]	generic, Roche, H2	X*	X*				X*		
diazepam nasal spray‡ (Valtoco®)[10]	Neurelis								
diazepam rectal gel (Diastat®)[11]	generic§, Bausch								
midazolam nasal spray‡ (Nayzilam®)[12]	UCB								

* Adult and pediatric indication

† Indicates approval for adjuvant therapy only

‡ Approved under the United States (US) Food and Drug Administration (FDA) 505(b)(2) pathway that allows at least some of the information submitted for approval to be from studies not conducted by or for the applicant

§ Available as an authorized generic (AG)

Anticonvulsants

FDA-Approved Indications (continued)

Drug	Manufacturer	Seizure Disorders				Neuropathic Pain	Lennox-Gastaut Syndrome	Migraine Prophylaxis	Bipolar Disorder
		Absence	Myoclonic	Partial	Tonic-Clonic				
Carbamazepine Derivatives									
carbamazepine (Tegretol®)[13]	generic, Novartis			X*	X*	X (associated with trigeminal neuralgia)			
carbamazepine extended-release (Tegretol® XR)[14]	generic, Novartis			X*	X*	X (associated with trigeminal neuralgia)			
carbamazepine extended-release (Carbatrol®)[15]	generic, Shire			X*	X*	X (associated with trigeminal neuralgia)			
carbamazepine extended-release (Equetro®)[16]	Validus			X*	X*	X (associated with trigeminal neuralgia)			X
eslicarbazepine (Aptiom®)[17]	Sunovion			X*					
oxcarbazepine (Trileptal®)[18]	generic, Novartis			X*					
oxcarbazepine extended-release (Oxtellar XR®)[19]	Supernus			X*					
Valproic Acid and Derivatives									
divalproex delayed-release (Depakote®)[20]	generic, Abbvie	X*	X	X	X			X	X
divalproex sodium extended-release (Depakote ER®)[21]	generic, Abbvie	X*		X*				X	X
valproic acid[22]	generic	X*	X*	X*	X*				

* Adult and pediatric indication

Anticonvulsants

FDA-Approved Indications (continued)

Drug	Manufacturer	Seizure Disorders				Neuropathic Pain	Lennox-Gastaut Syndrome	Migraine Prophylaxis	Bipolar Disorder
		Absence	Myoclonic	Partial	Tonic-Clonic				
Other Anticonvulsants									
brivaracetam (Briviact®)[23]	UCB			X*					
cannabidiol (Epidiolex®)[24]	Jazz						X*		
cenobamate (Xcopri®)[25]	SK Life Science			X					
felbamate (Felbatol®)[26]	generic, Meda/Mylan Specialty			X*¶			X†		
fenfluramine‡ (Fintepla®)[27]	Zogenix						X*		
gabapentin (Neurontin®)[28]	generic, Pfizer/Viatris			X*†		X (post herpetic neuralgia [PHN])			
ganaxolone (Ztalmy®)[29]	Marinus								
lacosamide (Vimpat®)[30]	generic, UCB			X*	X*†				
lacosamide extended-release (Motpoly XR™)[31]	Aucta			X*‖					
lamotrigine (Lamictal®, Lamictal® ODT)[32]	generic, GSK			X*	X*†		X*†		X**
lamotrigine XR (Lamictal® XR)[33]	generic, GSK			X*†	X*				
levetiracetam (Keppra®)[34]	generic, UCB		X*†	X*	X*†				
levetiracetam (Spritam®)[35]	Aprecia		X*†	X*	X*†				

* Adult and pediatric indication

† Indicates approval for adjuvant therapy only

‡ Approved under the FDA's 505(b)(2) pathway that allows at least some of the information submitted for approval to be from studies not conducted by or for the applicant

¶ Felbamate (Felbatol) is not indicated as first-line antiepileptic treatment and is recommended for use only in patients who respond inadequately to alternative treatments and whose epilepsy is so severe that a substantial risk of aplastic anemia and/or liver failure is deemed acceptable in relation to benefits

‖ Lacosamide extended-release (Motpoly XR) is indicated for adults and pediatric patients weighing ≥ 50 kg

** Lamotrigine (Lamictal) is not recommended for the treatment of acute manic or mixed episodes. The effectiveness of lamotrigine has not been established for the acute treatment of mood episodes.

Anticonvulsants

FDA-Approved Indications (continued)

Drug	Manufacturer	Seizure Disorders				Neuropathic Pain	Lennox-Gastaut Syndrome	Migraine Prophylaxis	Bipolar Disorder
		Absence	Myoclonic	Partial	Tonic-clonic				
Other Anticonvulsants (*continued*)									
levetiracetam XR‡ (Elepsia® XR)[36]	Tripoint			X*†					
levetiracetam XR (Keppra XR®)[37]	generic, UCB			X*					
perampanel (Fycompa®)[38]	Eisai, Catalyst			X*	X*†				
pregabalin (Lyrica®)[39]	generic, Pfizer/Viatris			X*†		X (associated with diabetic peripheral neuropathy, spinal cord injury, or PHN)			
rufinamide (Banzel®)[40]	generic, Eisai						X*†		
stiripentol (Diacomit®)[41]	Biocodex								
tiagabine (Gabitril®)[42]	generic, Cephalon			X*†					
topiramate (Topamax®)[43]	generic, Janssen			X*	X*		X*†	X*	
topiramate solution (Eprontia™)[44]	Azurity			X*	X*		X*†	X*	
topiramate XR (Qudexy® XR)[45]	generic, Upsher-Smith			X*	X*		X*†	X*	
topiramate XR (Trokendi XR®)[46]	generic, Supernus			X*	X*		X*†	X*	
vigabatrin (Sabril®)[47]	generic, Lundbeck			X*†					
zonisamide (Zonegran®)[48]	generic, Concordia			X*†					
zonisamide (Zonisade™)‡[49]	Azurity			X*†					

* Adult and pediatric indication
† Indicates approval for adjuvant therapy only
‡ Approved under the FDA's 505(b)(2) pathway that allows at least some of the information submitted for approval to be from studies not conducted by or for the applicant

Anticonvulsants

Other Epilepsy Indications

- Phenytoin (Dilantin, Phenytek) is indicated for prevention and treatment of seizures occurring during or following neurosurgery
- Diazepam nasal spray (Valtoco), diazepam rectal gel (Diastat), and midazolam nasal spray (Nayzilam) are indicated for the acute treatment of intermittent, stereotypic episodes of frequent seizure activity (e.g., seizure clusters, acute repetitive seizures) that are distinct from the patient's typical seizure pattern
- Oral diazepam tablets, solution, and concentrate and oral clorazepate are approved for the adjunctive treatment of seizure disorders

Anticonvulsants

Other Epilepsy Indications

- Carbamazepine (Equetro) is also approved for mixed-type seizures
- Cannabidiol solution (Epidiolex) is also approved for the treatment of seizures associated with Dravet syndrome and seizures associated with tuberous sclerosis complex
- Fenfluramine (Fintepla) is approved for the treatment of seizures associated with Dravet syndrome
- Ganaxolone (Ztalmy) is the first drug approved for the treatment of seizures associated with cyclin-dependent kinase-like 5 (CDKL5) deficiency disorder (CDD). It is indicated for use in patients ≥ 2 years of age
- Pregabalin (Lyrica) is also indicated for treatment of fibromyalgia. Pregabalin extended-release (ER; Lyrica CR) was approved in 2018 for the treatment of neuropathic pain associated with diabetic peripheral neuropathy and for post-herpetic neuralgia. It is, however, not indicated to treat seizure disorders and will not be discussed in this class review
- Vigabatrin (Sabril) is also indicated as monotherapy for the treatment of infantile spasms in infants 1 month to 2 years of age and when the potential benefit outweighs the risk of potential vision loss

Anticonvulsants

- Epilepsy affects 3.4 million Americans
- The 2018 American Academy of Neurology (AAN) guideline suggests that lamotrigine, levetiracetam, and zonisamide may be considered effective for patients with new-onset focal epilepsy
- In adults ≥ 60 years of age, lamotrigine *should* be considered, and gabapentin *may* be considered for new-onset focal epilepsy
- Consideration of immediate- and extended-release lamotrigine is recommended for adult patients with treatment-resistant generalized tonic-clonic seizures
- Ethosuximide or a valproic acid derivative should be considered before lamotrigine in newly diagnosed childhood absence epilepsy

Anticonvulsants

- For adults and children with Lennox-Gastaut syndrome, AAN recommends lamotrigine and topiramate
- There are several agents that are FDA-approved as adjunct therapy for this indication
- Clonazepam may be used as monotherapy or adjunctive therapy
- Felbamate should be reserved for use if all other options have been exhausted, and the benefits outweigh the risks of aplastic anemia and hepatotoxicity
- For treatment of infantile spasms, AAN recommends low-dose adrenocorticotropic hormone (ACTH) as the treatment of choice; vigabatrin may be useful for short-term treatment

Anticonvulsants

- Cannabidiol (Epidiolex) is FDA-approved for use in children and adults with Dravet syndrome and seizures associated with tuberous sclerosis complex
- It has not been addressed in guidelines yet, but it may be an option for adjunctive therapy in patients who experience refractory seizures with these conditions
- Stiripentol (Diacomit) is indicated for the treatment of seizures associated with Dravet syndrome when used with clobazam
- Fenfluramine (Fintepla) is also indicated for the treatment of seizures due to Dravet syndrome
- Ganaxolone (Ztalmy) is the first and only drug approved for the treatment of seizures associated with CDKL5 deficiency disorder (CDD)

Anticonvulsants

- If seizure control is not achieved with a single drug, an alternative medication should be attempted before others are added to current therapy
- Serum plasma levels, available with some drugs within this class, may assist in ensuring proper drug exposure and compliance
- Anticonvulsants have very little or no direct comparative data in the treatment of seizures or any other indication
- Overall, agents in this class have similar efficacy with the newer drugs generally having fewer serious adverse effects and drug interactions

Anticonvulsants

Product/Guideline Updates:

- Mylan has made a business decision to discontinue Felbatol oral suspension (600 mg/5 mL)

- The FDA has issued a Drug Safety Communication on the potential for life-threatening Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) reactions with levetiracetam (Keppra, Keppra XR, Elepsia XR, Spritam) and clobazam (Onfi, Sympazan).
  - The new warnings about DRESS will be added to the PI for these products
  - Symptoms usually start 2 weeks to 8 weeks after initiation, but could occur earlier or later.
  - Patients who experience any unusual symptoms, including rash, at any time while using these drugs should immediately seek emergency care
  - Although fever with rash and swollen lymph nodes or swelling in the face are common, some individuals do not develop a rash

Anticonvulsants

Product/Guideline Updates:

- Diazepam (Libervant) has been approved by the FDA for acute treatment of intermittent, stereotypic episodes of frequent seizure activity (e.g., seizure clusters, acute repetitive seizures) that are distinct from a patient's usual seizure pattern in patients with epilepsy 2 to 5 years of age
- Product will be available as a 5 mg, 7.5 mg, 10 mg, 12.5 mg, & 15 mg buccal film
- The recommended dosage is weight-based & administered by a caregiver
- Libervant should not be used to treat > 1 episode every 5 days or > 5 episodes per month
- Libervant has boxed warnings for risks from concomitant use with opioids; abuse, misuse, and addiction; & dependence and withdrawal reactions
- This product is schedule C-IV

Anticonvulsants

Product/Guideline Updates:

- Endo has voluntarily recalled 1 lot of clonazepam orally disintegrating tablets in the strength of 0.25 mg due to mislabeling (incorrect strength appears on the cartons of some packs showing the strength as 0.125 mg and not 0.25 mg). The blister strips inside the product packaging does reflect the correct 0.25 mg strength. Source: https://www.fda.gov/safety/recalls-market-withdrawals-safety-alerts/endo-usa-inc-issues-voluntary-nationwide-recall-one-lot-clonazepam-orally-disintegrating-tablets-usp

Antifungals, Oral

Antifungals, Oral

Class Overview - Product indications include*:

- Candidiasis (esophageal, oropharyngeal, and vaginal)
- Cryptococcal infections
- Tinea topical infections
- Onychomycosis
- Invasive aspergillosis

Not inclusive of all product indications, all products differ in indication

Antifungals, Oral

Class Overview:

- clotrimazole troche - (clotrimazole troche)
- fluconazole - (Diflucan, fluconazole)
- flucytosine - (Ancobon, flucytosine)
- griseofulvin suspension - (griseofulvin suspension)
- griseofulvin microsized - (griseofulvin microsized)
- griseofulvin ultramicrosized - (griseofulvin ultramicrosized)
- ibrexafungerp - (Brexafemme)
- isavuconazonium - (Cresmba)
- itraconazole - (itraconazole, Onmel, Sporanox)
- itraconazole – (Tolsura)
- ketoconazole - (ketoconazole)
- miconazole - (Oravig)
- nystatin - (nystatin)
- posaconazole - (Noxafil)
- terbinafine - (terbinafine)
- voriconazole - (Vfend, voriconazole)

Antifungals, Oral

- Antifungal agents have different spectrums of activity and are FDA-approved to treat a variety of infections
- Oral antifungal agents are useful in the treatment of a variety of infections in both immunocompetent and immunocompromised patients
- Few trials have been performed to compare safety and efficacy profiles of the drugs
- Many of the agents carry boxed warnings related to adverse events and/or drug interactions
- After bacterial vaginal infections, Vulvovaginal Candidiasis (VVC) is the second most common type of vaginal infection in the US
- It is estimated that treatment with azole antifungals provides relief of symptoms and negative cultures in 80% to 90% of patients with uncomplicated VVC

Antifungals, Oral

- Due to its excellent penetration into many tissues, fluconazole is an effective *Candida* treatment for a variety of infections, lacking concerns about pH-dependent absorption such as that seen with ketoconazole
- Effective therapy for oropharyngeal candidiasis includes fluconazole, itraconazole, ketoconazole, nystatin, and clotrimazole
- Voriconazole has been shown to have similar efficacy to fluconazole in the treatment of esophageal candidiasis; however, more adverse effects are reported with voriconazole
- Posaconazole oral suspension has an indication for treatment of oropharyngeal candidiasis when refractory to itraconazole and/or fluconazole

Antifungals, Oral

- Posaconazole delayed-release oral tablets are indicated to treat invasive aspergillosis
- Nystatin is also used to treat intestinal candidiasis and may be used in infants and children
- Isavuconazonium, posaconazole, flucytosine, voriconazole, itraconazole, and fluconazole have indications for the treatment and/or prophylaxis of various serious fungal infections

Antifungals, Oral

Clinical and Product Updates

- FDA posted that Pfizer will discontinue manufacture of Diflucan 50 mg, 100 mg, 150 mg, and 200 mg tablets
    - Generics remain

- Merck will discontinue the manufacture of brand Noxafil 100 mg DR tablets
    - Generics remain

Antifungals, Topical

Antifungals, Topical

Class Overview - Product indications include*:

- Cutaneous Candidiasis
- Tinea Pedis
- Tinea Corporis
- Tinea Cruris
- Tenia Versicolor
- Topical Onychomycosis
- Seborrheic Dermatitis

Not inclusive of all product indications, all products differ in indication

Antifungals, Topical

Class Overview

- butenafine - (Mentax)
- butenafine - (butenafine [OTC], Lotrimin Ultra [OTC])
- ciclopirox 0.77% - (Ciclodan Cream, Kit; ciclopirox cream; Loprox Cream, Gel, Suspension)
- ciclopirox 1% - (ciclopirox 1% shampoo, Loprox)
- ciclopirox 8% - (Ciclodan Solution, ciclopirox 8%)
- clotrimazole - (Alevazol [OTC], clotrimazole [OTC], Lotrimin AF [OTC], Micotrin AC[OTC], Mycozyl AC [OTC]), Votriza-AL® [OTC])
- clotrimazole/betamethasone - (clotrimazole/betamethasone)
- econazole cream - (econazole)

Antifungals, Topical

Class Overview:

- econazole foam - (Ecoza)
- efinaconazole - (Jublia)
- ketoconazole - (Extina, ketoconazole, Ketodan, Nizoral A-D 1% Shampoo [OTC], Xolegel)
- luliconazole - (Luzu)
- miconazole - (Azolen [OTC], Desenex [OTC] , Fungoid [OTC], Lotrimin AF Spray, [OTC], miconazole [OTC], Micotrin AP [OTC], Mycozyl AP [OTC], Zeasorb AF [OTC])
- miconazole/zinc oxide/white petrolatum - (Vusion)
- naftifine - (naftifine, Naftin)

Antifungals, Topical

Class Overview

- nystatin - (nystatin)
- nystatin/triamcinolone - (nystatin/triamcinolone)
- oxiconazole - (oxiconazole, Oxistat)
- sertaconazole - (Ertazco)
- sulconazole - (Exelderm)
- tavaborole - (Kerydin)
- terbinafine - (Lamisil [OTC], Lamisil AT [OTC], terbinafine [OTC])
- tolnaftate - (Fungoid-D [OTC], Micotrin AL [OTC], Mycozyl AL [OTC]), Ting [OTC], Lamisil AF Defense [OTC], Tinactin [OTC], tolnaftate [OTC])
- undecylenic acid - (Hongo Cura, Sponix Anti-Fungal [OTC])
- undecylenic acid/zinc undecylenic - (Fungi-Nail [OTC], Hongo Cura [OTC])

Antifungals, Topical

- Topical antifungal agents have different spectrums of activity and are FDA-approved to treat a variety of infections
- Topical agents may be formulated as creams, foams, gels, lacquers, lotions, ointments, powders, solutions and sprays
- Many topical antifungal preparations are available as prescription medications and over-the-counter (OTC) products
- Limited data are available regarding comparative efficacy in the treatment of the various fungal infections — tinea cruris, tinea corporis, tinea pedis, and tinea versicolor
- Combination therapy (antifungal plus corticosteroid) can be considered when inflammation is present

Antifungals, Topical

- Data are also lacking in comparative efficacy for the treatment of seborrheic dermatitis
- Based on limited efficacy data, choice of therapy is mainly based on clinical judgment regarding prior treatments and complicating conditions, such as bacterial growth or intense inflammation

Antimigraine Agents, Triptans

Antimigraine Agents, Triptans

Class Overview:

- almotriptan malate - (almotriptan)
- eletriptan - (eletriptan; Relpax)
- frovatriptan - (frovatriptan; Frova)
- naratriptan - (naratriptan)
- rizatriptan - (Maxalt, Maxalt MLT; rizatriptan ODT & tablet)
- sumatriptan - (Imitrex Kit, Tablet & Vial; Imitrex Nasal; sumatriptan kit, nasal, tablet & vial; Onzetra Xsail; Sumavel DosePro; Zembrace SymTouch)
- sumatriptan/naproxen - (sumatriptan/naproxen; Treximet)
- sumatriptan camphor/menthol - (Migranow)
- zolmitriptan - (zolmitriptan ODT, ODT (AG), tablets, tablets (AG), nasal spray; Zomig)

Antimigraine Agents, Triptans

- Migraines account for 10% to 20% of all headaches in adults and affect over 39 million men, women, and children in the United States
- Migraine headaches must be differentiated from regular tension-type headaches.
- Key criteria for migraine diagnosis include an episodic headache lasting from 4 to 72 hours with at least two of the following: unilateral pain, throbbing, aggravation of pain upon moving, pain of moderate to severe intensity accompanied by nausea, vomiting, photophobia, or phonophobia
- Non-opioid analgesia with acetaminophen, nonsteroidal anti-inflammatory drugs (NSAIDs), or caffeinated combinations are considered first-line therapy for mild to moderate migraine pain

Antimigraine Agents, Triptans

- Migraine-specific agents (triptans, dihydroergotamine [DHE]) should be used in patients who experience moderate to severe migraine attacks
- Due to well-established efficacy, triptans have become the drugs of choice for treating acute migraine attacks
- The US Headache Consortium, a multidisciplinary panel of several professional organizations, recognized that all of the triptans are effective agents for the acute treatment of migraine
- Data reviewed did not demonstrate that any specific triptan was superior to others and triptans appear to be equally safe

Antimigraine Agents, Triptans

- Per the American Academy of Neurology (AAN) and the American Headache Society (AHS), for pharmacologic treatment for episodic migraine prevention in adults:
    - Antiepileptic drugs (divalproex sodium, sodium valproate, topiramate) and beta-blockers (metoprolol, propranolol, timolol) are considered *effective* in migraine prevention
    - Naratriptan, zolmitriptan, antidepressants (amitriptyline, venlafaxine), and beta-blockers (atenolol, nadolol) are considered *probably effective* in migraine prevention
    - Frovatriptan is established for short-term menstrually-associated migraine (MAM) prevention

Antimigraine Agents, Triptans

- In addition to approval in adults, almotriptan, sumatriptan/naproxen, and zolmitriptan nasal spray are FDA-approved for use in patients 12 to 17 years old while rizatriptan is approved in patients 6 to 17 years old
- Non-oral routes of administration are available when nausea or vomiting present as significant components of migraine attacks

Antimigraine Agents, Triptans

Clinical and Product Updates

- FDA is reporting discontinuation of Imitrex 5 mg & 20 mg nasal spray by GlaxoSmithKline
- The last date that product was available for ordering was Jan 31, 2024
- Generics remain

Beta Blockers

Beta Blockers

Class Overview - Product indications include*:

- Hypertension
- Heart Failure
- Angina pectoris
- Myocardial Infarction
- Cardiac Arrhythmias
- Migraine Prophylaxis
- Tremor
- Hypertrophic subaortic stenosis

Not inclusive of all product indications, all products differ in indication

Beta Blockers

Class Overview: Single Agents

- acebutolol - (acebutolol, Sectral)
- atenolol - (atenolol, Tenormin)
- betaxolol - (betaxolol)
- bisoprolol - (bisoprolol)
- carvedilol - (carvedilol, Coreg)
- carvedilol extended-release - (carvedilol ER, Coreg CR)
- labetalol - (labetalol)
- metoprolol succinate ER - (metoprolol succinate ER, Toprol XL, Kapspargo Sprinkle)
- metoprolol tartrate - (Lopressor, metoprolol tartrate)
- nadolol - (Corgard, nadolol)
- nebivolol – (nebivolol)
- pindolol - (pindolol)
- propranolol - (propranolol)
- propranolol - (Hemangeol)
- propranolol ER - (Inderal XL, Innopran XL)
- propranolol LA - (Inderal LA, propranolol LA)
- sotalol - (Betapace, sotalol)
- sotalol - (Betapace AF, sotalol AF)
- sotalol - (Sotylize)
- timolol - (timolol)

Beta Blockers

Class Overview: Beta-Blocker/Diuretic Combinations

- atenolol/chlorthalidone - (atenolol/chlorthalidone, Tenoretic)
- bisoprolol/HCTZ - (bisoprolol/HCTZ , Ziac)
- metoprolol succinate/HCTZ - (Dutoprol, metoprolol succinate/HCTZ)
- metoprolol tartrate/HCTZ - (metoprolol tartrate/HCTZ)
- nadolol/bendroflumethiazide - (Corzide, nadolol/bendroflumethiazide)
- propranolol/HCTZ - (propranolol/HCTZ)

Beta Blockers

- Approximately 120 million (48%) of adults in the United States have hypertension (HTN)
- Highest prevalence is among African American adults and men at 56% and 50%, respectively
- It is estimated that hypertension is controlled in only 22.5% of patients with the condition
- Hypertension is an independent risk factor for the development of cardiovascular disease (CVD)
- Beta-blockers are one of the classes suggested as first-line therapy in patients with coronary artery disease (CAD), post-MI, and HF

Beta Blockers

- Beta-blockers have similar efficacy for the treatment of HTN
- The Eighth Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC-8) does not recommend beta-blockers as initial treatment for hypertension
- This is due to a demonstrated higher rate of the primary composite outcome of CV death, MI, or stroke compared to use of an ARB with beta blocker use, a finding that was driven largely by an increase in stroke
- Beta-blockers prevent recurrent ischemia, life-threatening ventricular arrhythmias, reduce the incidence of sudden cardiac death and improve survival in patients with prior MI

Beta Blockers

- The 2007 ACC/AHA chronic stable angina guidelines recommend indefinite beta-blocker therapy for blood pressure control in patients with CAD, acute coronary syndrome (ACS), or left ventricular dysfunction (LVD), with or without heart failure symptoms
- Beta-blockers have also been shown to reduce mortality in patients with chronic heart failure (bisoprolol, carvedilol, and metoprolol succinate extended-release)

BPH Treatments

BPH Treatments

Class Overview: Alpha-Blockers

- alfuzosin ER - (alfuzosin ER, Uroxatral)
- doxazosin - (Cardura, doxazosin)
- doxazosin ER - (Cardura XL)
- silodosin - (Rapaflo, silodosin)
- tamsulosin - (Flomax, tamsulosin)
- terazosin - (terazosin)

BPH Treatments

Class Overview: 5-Alpha Reductase (5AR) Inhibitors

- dutasteride - (Avodart, dutasteride)
- finasteride - (finasteride, Proscar)

Class Overview: 5-Alpha Reductase (5AR) Inhibitor/Alpha Blocker Combinations

- dutasteride/tamsulosin - (dutasteride/tamsulosin, Jalyn)

Class Overview: Phosphodiesterase 5 (PDE5) Inhibitors

- tadalafil - (Cialis, tadalafil)

BPH Treatments

Class Overview: **5-Alpha Reductase (5AR) Inhibitor / Phosphodiesterase 5 (PDE5) Inhibitor Combinations**

- finasteride/tadalafil - (Entadfi)

BPH Treatments

- Benign prostatic hyperplasia (BPH) is one of the most common conditions in aging men
- Approximately 14 million men in the US have symptoms related to BPH
- An estimated 50% of men demonstrate histopathologic BPH by age 60 years; this etiology increases to 90% by 85 years of age
- Drugs used in the treatment of BPH relieve lower urinary tract symptoms (LUTS) and prevent complications and, in some cases, are an alternative to surgical intervention
- All products are indicated for the treatment of symptomatic BPH but none are indicated for prevention of prostate cancer
- Various products carry other non-BPH indications

BPH Treatments

- The 2021 American Urological Association (AUA) state that alfuzosin (Uroxatral), doxazosin (Cardura), silodosin (Rapaflo), tamsulosin (Flomax), and terazosin should be offered for patients with bothersome, moderate to severe LUTS/BPH
- When an alpha- blocker is chosen, the specific choice should be based on patient age, comorbidities, and the adverse event profiles of the specific medication
- Equal efficacy for all alpha-blockers has been demonstrated regarding various subsets of patients
- It is not recommended to switch between different alpha-blockers if a patient fails to have adequate improvement with the first agent at an appropriate dose
- However, switching alpha-blockers can be done to improve an adverse effect, if needed

BPH Treatments

- The AUA recommends that when alpha-blocker therapy is started, patients with planned cataract surgery are informed of the potential risks regarding intraoperative floppy iris syndrome and should discuss these risks with their ophthalmologist
- The guidelines also state that the 5-alpha reductase inhibitors, finasteride (Proscar) and dutasteride (Avodart), should be used as a treatment option for patients with LUTS/BPH associated with demonstrable prostatic enlargement
- The 5ARs alone or in combination with alpha-blockers may be used to prevent progression of LUTS/BPH and to reduce the risk of urinary retention and future prostate-related surgery

BPH Treatments

- 5ARs can also be considered to reduce intraoperative bleeding and peri- or postoperative need for blood transfusion after transurethral resection of the prostate (TURP) or other surgical intervention for BPH
- In regard to the PDE5 inhibitor tadalafil, for patients with LUTS/BPH, regardless of comorbid erectile dysfunction (ED), 5 mg daily tadalafil is a potential treatment option
- 5ARs can be used in combination with an alpha-blocker for patients with LUTS associated with demonstrable prostatic enlargement
- However, the combination of low-dose 5 mg daily tadalafil with an alpha-blocker for LUTS/BPH should not be used, as it does not offer an advantage for symptom improvement over either agent alone

BPH Treatments

- For patients with LUTS associated with demonstrable prostatic enlargement, the AUA gives a strong recommendation that the combination of a 5-alpha reductase inhibitor and an alpha-blocker may be considered
- However, the combination of low-dose 5 mg daily tadalafil with an alpha-blocker or finasteride for LUTS/BPH gets only a conditional recommendation, as data have not drawn any definite conclusions

BPH Treatments

- 5ARs are not to be administered to women or children
- Women who are pregnant or who may become pregnant should not handle dutasteride capsules or finasteride tablets

Calcium Channel Blockers

Calcium Channel Blockers

Class Overview - Product indications include*:

- Hypertension
- Angina
- Vasospastic Angina
- Ventricular Rate Control
- Unstable Angina
- Coronary Artery Disease
- Subarachnoid hemorrhage

Not inclusive of all product indications, all products differ in indication

Calcium Channel Blockers

Class Overview: Dihydropyridines

- amlodipine - (amlodipine, Norvasc, Norliqva)
- felodipine ER - (felodipine ER, Plendil)
- isradipine - (isradipine)
- nicardipine - (Cardene, nicardipine)
- nicardipine SR - (Cardene SR)
- nifedipine - (nifedipine, Procardia)
- nifedipine ER, SA, SR - (Adalat CC; Afeditab CR; Nifediac CC; Nifedical XL nifedipine ER, SA, SR; Procardia XL)
- nimodipine - (nimodipine)

Calcium Channel Blockers

Class Overview: Dihydropyridines

- nimodipine solution - (Nymalize)
- nisoldipine ER- (nisoldipine ER, Sular)

Class Overview: Non-dihydropyridines

- diltiazem - (Cardizem, diltiazem)
- diltiazem ER - (Cardizem LA, diltiazem ER, Matzim LA)
- diltiazem ER - (Cardizem CD; Cartia XT; diltiazem ER; Dilacor XR; Dilt CD; Taztia XT; Tiazac)

Calcium Channel Blockers

Class Overview: Non-dihydropyridines

- diltiazem ER - (Dilt XR, Diltia XT)
- verapamil - (Calan, verapamil)
- verapamil ER - (Covera-HS)
- verapamil ER - (verapamil ER, Verelan PM)
- verapamil SR - (Calan SR, Isoptin SR, verapamil ER, Verelan)

Calcium Channel Blockers

- Calcium channel blockers (CCBs) are widely used in the treatment of hypertension and angina pectoris
- Per the JNC-8, first-line therapy for HTN in the non-African American population is a thiazide-type diuretic, a CCB, an ACE inhibitor, or an angiotensin receptor blocker (ARB)
- They recommend a thiazide diuretic or CCB for African Americans
- The benefits of CCBs in controlling angina and hypertension have been clearly documented
- No CCB has demonstrated a clinical advantage over other CCBs in the treatment of hypertension
- Dihydropyridine CCBs may cause a baroreceptor-mediated reflex increase in heart rate because of their potent peripheral vasodilating effects

Calcium Channel Blockers

- Diltiazem decreases atrioventricular conduction and heart rate
- Verapamil decreases heart rate, slows atrioventricular nodal conduction to the greatest extent of the CCBs, and is useful for supraventricular tachyarrhythmias
- Short-acting nifedipine has been related to increased coronary mortality rates in patients with a history of MI and should not be used for the treatment of hypertension
- The ALLHAT study enrolled patients with hypertension and with a known risk factor for CAD
- The study showed that chlorthalidone, amlodipine, and lisinopril had similar outcomes of combined fatal coronary heart disease (CHD) and nonfatal MI

Calcium Channel Blockers

- Many large trials enrolling patients with hypertension have demonstrated that CCBs have beneficial effects on composite cardiovascular outcomes or individual clinical outcomes
- However, most of the trials only demonstrated equivalence to the comparator antihypertensives rather than superiority

Contraceptives

Contraceptives

Class Overview – Combined Pill:

desogestrel/ethinyl estradiol
APRI
AZURETTE
CAZIANT
OCELLA
ethynodiol diacetate/ethinyl estradiol
KELNOR
levonorgestrel/ethinyl estradiol
AMETHIA LO
AMETHYST
AUBRA
ENPRESSE

Contraceptives, Oral

Class Overview – Combined Pill (cont.):

norethindrone acetate/ethinyl estradiol	
BALZIVA	KAITLIB, FE
CYCLAFEM	LOESTRIN, FE
ESTARYLLA	MELODETTA
ESTROSTEP	NECON
GILDESS	ORTHO TRI-CYCLEN
JUNEL, FE	

Contraceptives

- ***Class Overview: Combination Contraceptives- Vaginal***
  - ***etonogestrel-ethinyl estradiol ring (Nuvaring)***

- ***Class Overview: Copper Contraceptives - IUD***
  - ***copper IUD (Paragard)***

- ***Class Overview: Emergency Contraceptives***
  - ***levonorgestrel (Emergency OC) Tablets – Plan B One-Step OTC***
  - ***levonorgestrel (Emergency OC) Tablets- Aftera OTC***
  - ***levonorgestrel (Emergency OC) Tablets- My Choice OTC***
  - ***levonorgestrel (Emergency OC) Tablets- My Way OTC***
  - ***levonorgestrel (Emergency OC) Tablets- New Day OTC***
  - ***levonorgestrel (Emergency OC) Tablets- Option 2 OTC***
  - ***ulipristal acetate tablets- Ella***

Contraceptives

- ***Class Overview: Combination Progestins***
  - ***medroxyprogesterone acetate tablets (Provera)***
  - ***norethindrone acetate (Aygestin)***
  - ***progesterone micronized capsules (Prometrium)***

- ***Class Overview: Progestin Contraceptives - Implants***
  - ***etonogestrel Implant (Nexplanon)***

- ***Class Overview: Progestin Contraceptives - Injectable***
  - ***medroxyprogesterone acetate (contraceptive) suspension – Depo-Provera Contraceptive***

Contraceptives

- ***Class Overview: Progestin IUD***
  - ***levonorgestrel (IUD) – Liletta***
  - ***levonorgestrel (IUD) – Skyla***
  - ***levonorgestrel (IUD) – Mirena***
  - ***levonorgestrel (IUD) – Kyleena***

- ***Class Overview: Progestin Contraceptives – Oral***
  - ***norethindrone (Contraceptive) Tablets – Camila***

- ***Class Overview: Progestin Contraceptives – Transdermal***
  - ***norelgestromin-ethinyl estradiol patch weekly – Xulane***

Contraceptives

- Hormonal oral contraceptives (OCs) are available in various dosage forms for prevention of pregnancy
- Combination oral contraceptives (COCs) contain estrogen and progestin, while progestin-only products contain progestin alone
- Products differ in the specific hormones they contain and how these hormones are dosed throughout the cycle (hormone phases) resulting in several product options which produce different cycle lengths and physiological effects
- Traditional OCs are administered daily for 21 days followed by a hormone-free week during which menstruation occurs
- Extended cycle products (e.g., 91-day cycle) delay or completely eliminate the break in hormone use and may be desirable to women who wish to avoid menstruation

Contraceptives

- Selection of the most appropriate product for a patient may depend on the desired phases of hormones, cycle length, associated product risks, side effect profile, and tolerability
- Hormones vary in their venous thrombosis risk, an important point to consider when selecting a product
- In addition, some OCs have additional indications or ingredients; for example, certain products are approved for the treatment of acne vulgaris or premenstrual dysphoric disorder (PMDD), and several products contain iron
- The Centers for Disease Control and Prevention (CDC) selected practice recommendations for contraceptive use continues to recommend COCs and progestin-only OCs as effective methods of contraception

Contraceptives

- Details on the appropriate selection of an effective contraceptive method (e.g., intrauterine device, implant, injection, OC) are described in CDC's published Medical Eligibility Criteria
- The CDC also provides guidance to improve family planning services in the United States (US), including the use of contraceptives
- In 2019, the American College of Obstetricians and Gynecologists (ACOG) published a bulletin regarding the use of hormonal contraception in women with medical conditions, confirming the Medical Eligibility Criteria and recommending appropriate use of the criteria for women with co-existing medical conditions who need contraception

Contraceptives

- ACOG also released an opinion statement in favor of over-the-counter (OTC) access for OCs without regard to age, stating that women are capable of self-screening and determining their own eligibility for OCs, with pharmacist-provided contraception as a possible intermediary step
- They also state that pelvic, breast, sexually transmitted infections (STIs), and cancer examinations and screenings should not be used as barriers to OCs
- ACOG states that long-acting reversible contraceptives (LARC) are safe and have higher rates of efficacy, continuation, and satisfaction compared with short-acting contraceptives; therefore, these are excellent contraceptive choices for adolescents
- COCs (estrogen/progestin) are generally grouped based on the dosage regimen strategy
  - Most are based on a 28-day monthly cycle and are available as monophasic, biphasic, triphasic, and 4-phase products
  - There are also extended-cycle products and a continuous-cycle product available

Hereditary Angioedema Agents

Hereditary Angioedema Agents

Drug	Manufacturer	Indication(s)
Prophylaxis		
berotralstat (Orladeyo™)[1]	BioCryst	Routine prophylaxis to prevent HAE attacks in ages ≥ 12 years
C1-esterase INH [Human] (Cinryze®)[2]	Viropharma	Routine prophylaxis to prevent HAE attacks in ages ≥ 6 years
C1-esterase INH [Human] (Haegarda®)[3]	CSL Behring	Routine prophylaxis to prevent HAE attacks in ages ≥ 6 years
lanadelumab-flyo (Takhzyro®)[4]	Takeda	Routine prophylaxis to prevent HAE attacks in ages ≥ 12 years

Hereditary Angioedema Agents

Treatment		
ecallantide (Kalbitor®)[5]	Dyax/Shire	Treatment of acute HAE attacks in ages ≥ 12 years
icatibant (Firazyr®)[6]	generic, Shire	Treatment of acute HAE attacks in ages ≥ 18 years
C1-esterase INH [Human] (Berinert®)[7]	CSL Behring	Treatment of acute HAE facial, laryngeal, or abdominal attacks in adult and pediatric patients Safety and efficacy for prophylactic therapy have not been established
rhC1-INH [recombinant] (Ruconest®)[8]	Santarus/Pharming Healthcare	Treatment of acute attacks in adult and adolescent patients with HAE Effectiveness has not been established in HAE patients with laryngeal attacks

C1-INH = C1 esterase inhibitor; HAE = hereditary angioedema

Berinert, Cinryze, and Haegarda are plasma-derived (pd) C1 esterase inhibitors. Ruconest is a recombinant (rh) analogue of human complement C1 esterase inhibitor.

Hereditary Angioedema Agents

- Hereditary angioedema (HAE) is a rare, dominant autosomal genetic disorder that affects approximately 6,000 individuals in the US
- Patients with HAE have low levels of endogenous or functional C1 esterase inhibitor (C1-INH)
- HAE is characterized by recurrent episodes of nonpruritic, nonpitting, subcutaneous (SC) or submucosal edema involving the skin or mucosal tissues of the upper respiratory and gastrointestinal (GI) tracts
- Although swelling can resolve spontaneously in several days, without treatment laryngeal edema may be fatal and the pain of GI attacks can be incapacitating

Hereditary Angioedema Agents

- Symptoms can begin as early as 2 years of age and persist throughout life with unpredictable severity and frequency of attacks
- It is thought that minor trauma and stress can lead to an attack; however, many attacks occur without any apparent trigger
- There are 2 types of C1-INH deficient HAE. The most common type (Type I), in which the body does not produce enough C1-INH, occurs in about 85% of patients with the condition
- Type II HAE is characterized by the presence of normal or high levels of a dysfunctional C1-INH

Hereditary Angioedema Agents

- HAE prophylaxis is needed to reduce potential edema caused by a stressor or procedure likely to precipitate an attack (short-term prophylaxis) or to decrease the number and severity of angioedema attacks (long-term prophylaxis)
- The 2020 US Hereditary Angioedema Association (HAEA) guidelines for the management of HAE recommends short-term prophylaxis prior to medical, dental, or surgical procedures
- As disease severity may change over time, the need for continued long-term prophylaxis should be assessed periodically. In addition, patients receiving prophylactic therapy should also have access to on-demand treatment for acute attacks
- The need for long-term prophylaxis should be made based on attack frequency, attack severity, comorbid conditions, access to treatment, and patient experience and preference

Hereditary Angioedema Agents

- The 2021 World Allergy Organization (WAO) and European Academy of Allergy and Clinical Immunology (EAACI) issued an update to the 2017 guidelines on the management of HAE
- The revised guidelines recommend Cinryze, Haegarda, Takhzyro, or Orladyeo as first line agents for long-term prophylaxis
- Androgens are suggested as second-line long-term prophylaxis
- HAE attacks should be treated with Berinert, Ruconest, Kalbitor, or Firazyr
- No one agent is recommended over another

Hereditary Angioedema Agents

- Plasma-derived concentrates of human plasma-derived C1-INH (Berinert, Cinryze) and a recombinant analogue of C1-INH (Ruconest) are available as IV injections, and human plasma-derived C1-INH (Haegarda) is available as a subcutaneous injection
- Ecallantide (Kalbitor) is a selective inhibitor of the plasma protein, kallikrein, and is administered subcutaneously
- Lanadelumab-flyo (Takhzyro) is the second kallikrein inhibitor, but the only monoclonal antibody, and is administered subcutaneously
- Berotralstat (Orladeyo) is the third kallikrein inhibitor and is administered orally once daily
- Icatibant (Firazyr) is a selective synthetic bradykinin B2 receptor antagonist and is also administered subcutaneously

Hereditary Angioedema Agents

Clinical and Product Updates

- FDA posted that Takeda (lanadelumab-flyo) will discontinue Takhzyro injection 300/2mL SDV
- This does not apply to the prefilled syringes

HIV - AIDS

HIV - AIDS

Drug	Manufacturer	Indication(s)
Attachment Inhibitor		
fostemsavir (Rukobia)[1]	Viiv	Treatment of human immunodeficiency virus type 1 (HIV-1) infection for use in combination with other antiretrovirals in heavily treatment-experienced adults with multidrug-resistant HIV-1 infection failing their current antiretroviral regimen due to resistance, intolerance, or safety considerations
Capsid Inhibitor		
lenacapavir (Sunlenca®)[2]	Gilead	Treatment of HIV-1 infection, in combination with other antiretroviral(s), in heavily treatment-experienced adults with multidrug resistant HIV-1 infection failing their current antiretroviral regimen due to resistance, intolerance, or safety considerations
C-C Chemokine Receptor 5 (CCR5) Antagonist		
maraviroc (Selzentry®), *MVC*[3]	Camber, Viiv	Combination antiretroviral treatment of adults and pediatric patients weighing ≥ 2 kg infected with only CCR5-tropic HIV-1
Fusion Inhibitor		
enfuvirtide (Fuzeon®), *T20* or *ENF*[4]	Genentech	Treatment of HIV-1 infection in treatment-experienced patients with evidence of HIV-1 replication despite ongoing antiretroviral therapy in combination with other antiretrovirals

HIV - AIDS

Integrase Strand Transfer Inhibitors (INSTIs)		
cabotegravir (Vocabria), *CBV*[5]	Viiv	▪ In combination with rilpivirine for short-term treatment of HIV-1 infection in adults and adolescents ≥ 12 years of age and weighing ≥ 35 kg who are virologically suppressed (HIV-1 RNA < 50 copies/mL) on a stable antiretroviral regimen with no history of treatment failure and with no known or suspected resistance to either cabotegravir or rilpivirine ▪ For use as either oral lead-in to assess the tolerability of cabotegravir prior to administration of cabotegravir/rilpivirine extended-release (ER) injectable suspensions or cabotegravir ER injectable suspension; or oral therapy for patients who will miss planned injection dosing with cabotegravir/rilpivirine ▪ For at-risk adults and adolescents weighing ≥ 35kg for short-term pre-exposure prophylaxis (PrEP) to reduce the risk of sexually acquired HIV-1 infection. Individuals must have a negative HIV-1 test prior to initiating for HIV-1 PrEP
cabotegravir ER* (Apretude), *CBV*[6]	Viiv	In at-risk adults and adolescents weighing ≥ 35 kg for PrEP to reduce the risk of sexually acquired HIV-1 infection. Individuals must have a negative HIV-1 test prior to initiating cabotegravir ER (with or without an oral lead-in with oral cabotegravir) for HIV-1 PrEP

* Available at an authorized generic.

HIV - AIDS

Drug	Manufacturer	Indication(s)
Integrase Strand Transfer Inhibitors (INSTIs) *(continued)*		
dolutegravir (Tivicay®, Tivicay PD®), *DTG*[7]	Viiv	▪ Tivicay and Tivicay PD: In combination with other antiretroviral agents for the treatment of HIV-1 infection in adults (treatment-naïve or -experienced) and in pediatric patients (treatment-naïve or -experienced but INSTI-naïve) aged ≥ 4 weeks and weighing ≥ 3 kg ▪ Tivicay *only*: In combination with rilpivirine as a complete regimen to replace the current antiretroviral regimen in those who are virologically suppressed (HIV-1 RNA < 50 copies/mL) on a stable antiretroviral regimen for ≥ 6 months with no history of treatment failure or known substitutions associated with resistance to either antiretroviral component
raltegravir (Isentress®, Isentress HD®), *RAL*[8]	Merck	In combination with other antiretroviral agents for the treatment of HIV-1 infection in patients weighing ≥ 2 kg†

HIV - AIDS

Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)		
doravirine (Pifeltro®), *DOR*[9]	Merck	In combination with other antiretroviral agents for the treatment of HIV-1 infection in adults and **pediatric patients weighing ≥ 35kg** with no prior antiretroviral treatment history or to replace the current antiretroviral regimen in those who are virologically suppressed (HIV-1 RNA < 50 copies/mL) on a stable antiretroviral regimen with no history of treatment failure and no known substitutions associated with resistance to doravirine
efavirenz (Sustiva®), *EFV*[10]	generic, Bristol-Myers Squibb	In combination with other antiretroviral agents for the treatment of HIV-1 infection in adults and pediatric patients ≥ 3 months of age who weigh ≥ 3.5 kg
etravirine (Intelence®), *ETR*[11]	generic, Janssen	In combination with other antiretroviral agents for the treatment of HIV-1 infection in treatment-experienced patients ≥ 2 years old
nevirapine, *NVP*[12]	generic	In combination with other antiretroviral agents for the treatment of HIV-1 infection in adults and in pediatric patients ≥ 15 days old
nevirapine ER, *NVP*[13]	generic	In combination with other antiretroviral agents for the treatment of HIV-1 infection in adults and in children ≥ 6 years of age with a body surface area (BSA) ≥ 1.17 m^2

HIV - AIDS

nevirapine ER, *NVP*[13]	generic	In combination with other antiretroviral agents for the treatment of HIV-1 infection in adults and in children ≥ 6 years of age with a body surface area (BSA) ≥ 1.17 m^2
rilpivirine (Edurant®), *RPV*[14]	Janssen	▪ In combination with other antiretroviral agents for the treatment of HIV-1 infection in treatment-naïve patients ≥ 12 years of age and weighing ≥ 35 kg with HIV-1 RNA ≤ 100,000 copies/mL ▪ In combination with cabotegravir (Vocabria) for short-term treatment of HIV-1 infection in adults and adolescents ≥ 12 years of age and weighing ≥ 35 kg who are virologically suppressed (HIV-1 RNA < 50 copies/mL) on a stable regimen with no history of treatment failure and with no known or suspected resistance to either cabotegravir or rilpivirine for use as: (1) oral lead-in to assess the tolerability of rilpivirine prior to administration of rilpivirine ER injectable suspension, a component of Cabenuva, or (2) oral therapy for patients who will miss planned injection dosing with Cabenuva

HIV - AIDS

Drug	Manufacturer	Indication(s)
Nucleoside Reverse Transcriptase Inhibitors (NRTIs)		
abacavir (Ziagen®), *ABC*[15]	generic, Viiv	In combination with other antiretroviral agents for the treatment of HIV-1 infection
didanosine, *ddI*[16]	Aurobindo	In combination with other antiretroviral agents for the treatment of HIV-1 infection
emtricitabine (Emtriva®), *FTC*[17]	Cipla, Gilead	In combination with other antiretroviral agents for the treatment of HIV-1 infection
lamivudine (Epivir®), *3TC*[18]	generic, Viiv	In combination with other antiretroviral agents for the treatment of HIV-1 infection *Limitation of Use:* The dosage of this product is for HIV and not for hepatitis B virus (HBV)
stavudine, *d4t*[19]	generic	In combination with other antiretroviral agents for the treatment of HIV-1 infection
zidovudine (Retrovir®), AZT20	generic, Viiv	▪ In combination with other antiretroviral agents for the treatment of HIV-1 infection ▪ Prevention of maternal-fetal HIV-1 transmission

HIV - AIDS

Nucleotide Reverse Transcriptase Inhibitor (NRTI)		
tenofovir disoproxil fumarate (Viread®), *TDF*[20]	generic, Gilead	In combination with other antiretroviral agents for the treatment of HIV-1 infection in adults and pediatric patients ≥ 2 years of age; Treatment of chronic hepatitis B (an infection with HBV) in adults ages ≥ 18 years and pediatric patients ≥ 2 years of age weighing ≥ 10 kg
Pharmacokinetic Enhancer		
cobicistat (Tybost®), *COBI* or *c*[21]	Gilead	In combination with atazanavir or darunavir to increase their systemic exposure once daily in combination with other antiretroviral agents in the treatment of HIV-1 infection in adults and in pediatric patients weighing ≥ 35 kg co-administered with atazanavir or weighing ≥ 40 kg co-administered with darunavir

HIV - AIDS

Protease Inhibitors (PIs)		
atazanavir (Reyataz®), *ATV*[23]	generic, Bristol-Myers Squibb	▪ In combination with other antiretroviral agents for the treatment of HIV-1 infection Treatment of HIV-1 infection in pediatric patients ≥ 3 years of age who weigh ≥ 5 kg
darunavir (Prezista®), *DRV*[24]	generic, Janssen	▪ Treatment of HIV-1 infection in adult patients, including pregnant women ▪ Treatment of HIV-1 infection in pediatric patients ≥ 3 years of age who weigh ≥ 10 kg *Limitation of use:* Prezista must be co-administered with ritonavir and with other antiretroviral agents
fosamprenavir (Lexiva®), *FPV*[25]	generic, Viiv	▪ In combination with other antiretroviral agents for the treatment of HIV-1 infection
nelfinavir (Viracept®), *NFV*[26]	Viiv	▪ In combination with other antiretroviral agents for the treatment of HIV-1 infection
ritonavir (Norvir®), *RTV* or *r*[27]	generic, Abbvie	▪ In combination with other antiretroviral agents for the treatment of HIV-1 infection

HIV - AIDS

Drug	Manufacturer	Indication(s)
Protease Inhibitors (PIs) *(continued)*		
tipranavir (Aptivus®), *TPV*[28]	Boehringer Ingelheim	Co-administered with ritonavir for combination antiretroviral treatment of HIV-1 infected patients who are treatment-experienced and infected with HIV-1 strains resistant to > 1 PI; not indicated for use in treatment-naïve patients
Recombinant Monoclonal Antibody		
ibalizumab-uiyk (Trogarzo®)[29]	Thera	In combination with other antiretroviral(s) for the treatment of HIV-1 infection in heavily treatment-experienced adults with multidrug-resistant HIV-1 infection failing their current antiretroviral regimen

HIV - AIDS

emtricitabine/tenofovir disoproxil fumarate (Truvada®), *FTC/TDF*[33]	generic, Gilead	A co-formulated product containing 2 NRTIs used in combination with other antiretroviral agents for the treatment of HIV-1 infection in adults and pediatric patients weighing ≥ 17 kg; Indicated in at-risk adults and adolescents weighing ≥ 35 kg for PrEP to reduce the risk of sexually acquired HIV-1 infection; individuals must have a negative HIV-1 test immediately prior to initiating Truvada for HIV-1 PrEP
lamivudine/tenofovir disoproxil fumarate (Cimduo®), *3TC/TDF*[34]	Mylan	A combination of 2 NRTIs indicated in combination with other antiretroviral agents for the treatment of HIV-1 infection in adults and pediatric patients weighing ≥ 35 kg
lamivudine/zidovudine (Combivir®), *3TC/AZT*[35]	generic, Viiv	A co-formulated product containing 2 NRTIs used in combination with other antiretroviral agents for the treatment of HIV-1 infection in adults and pediatric patients weighing ≥ 30 kg

HIV - AIDS

Combination Products – Protease Inhibitors (PIs) or PIs + Pharmacokinetic Enhancer		
atazanavir/cobicistat (Evotaz®), *ATV/c*[37]	Bristol-Myers Squibb	A co-formulated product containing a PI and a pharmacokinetic enhancer used in combination with other antiretroviral agents for the treatment of HIV-1 infection in adults and pediatric patients weighing ≥ 35 kg
darunavir/cobicistat (Prezcobix®), *DRV/c*[38]	Janssen	A co-formulated product containing a PI and a pharmacokinetic enhancer used in combination with other antiretroviral agents for the treatment of HIV-1 infection in treatment-naïve and treatment-experienced adults and pediatric patients weighing ≥ 40 kg with no darunavir resistance-associated substitutions (V11I, V32I, L33F, I47V, I50V, I54L, I54M, T74P, L76V, I84V, L89V)
lopinavir/ritonavir (Kaletra®), *LPV/r*[39]	generic, Abbvie	A co-formulated product containing 2 PIs used in combination with other antiretroviral agents for the treatment of HIV-1 infection in adults and pediatric patients (≥ 14 days old)

HIV - AIDS

Combination Products – Multiple Classes		
bictegravir/emtricitabine/ tenofovir alafenamide (Biktarvy®), *BIC/FTC/TAF*[39]	Gilead	As a complete regimen for the treatment of HIV-1 infection in adults and pediatric patients weighing ≥ 14 kg who have no antiretroviral treatment history or to replace the current antiretroviral regimen in those who are virologically suppressed (HIV-1 RNA < 50 copies/mL) on a stable antiretroviral regimen with no history of treatment failure and no known substitutions associated with resistance to the individual components
cabotegravir/rilpivirine, ER injection (Cabenuva), *CAB/RPV*[40]	Viiv	A co-packaged product containing an INSTI and NNRTI indicated as a complete regimen for the treatment of HIV-1 infection in adults and adolescents ≥ 12 years of age and weighing ≥ 35 kg to replace the current antiretroviral regimen in those who are virologically suppressed (HIV-1 RNA < 50 copies/mL) on a stable antiretroviral regimen with no history of treatment failure and with no known or suspected resistance to either cabotegravir or rilpivirine
darunavir/cobicistat/ emtricitabine/tenofovir alafenamide (Symtuza®), *DRV/c/FTC/TAF*[41]	Janssen	A co-formulated product containing a PI, a CYP3A inhibitor, and 2 NRTIs indicated as a complete regimen for the treatment of HIV-1 infection in adults and pediatric patients weighing ≥ 40 kg who have no prior antiretroviral treatment history or who are virologically suppressed (HIV-1 RNA < 50 copies/mL) while on stable antiretroviral therapy for ≥ 6 months and have no known substitutions associated with resistance to darunavir or tenofovir

HIV - AIDS

Combination Products – Multiple Classes		
dolutegravir/abacavir/ lamivudine (Triumeq, Triumeq PD), *DTG/ABC/3TC*[42]	Viiv	A co-formulated product containing 1 INSTI and 2 NRTIs indicated for the treatment of HIV-1 infection in adults and pediatric patients ≥ 3 months of age and weighing ≥ 6 kg
dolutegravir/lamivudine (Dovato®), *DTG/3TC*[43]	Viiv	A co-formulated product containing 1 INSTI and 1 NRTI indicated as a complete regimen for the treatment of HIV-1 infection in adults with no antiretroviral treatment history or to replace the current antiretroviral regimen in those who are virologically suppressed (HIV-1 RNA < 50 copies/mL) on a stable antiretroviral regimen with no history of treatment failure and no known substitutions associated with resistance to the individual components of Dovato
dolutegravir/rilpivirine (Juluca®), *DTG/RPV*[44]	Viiv	A co-formulated product containing 1 INSTI and 1 NNRTI indicated as a complete regimen for the treatment of HIV-1 infection in adults to replace the current antiretroviral regimen in those who are virologically suppressed (HIV-1 RNA < 50 copies/mL) on a stable antiretroviral regimen for ≥ 6 months with no history of treatment failure and no known substitutions associated with resistance to its individual components

HIV - AIDS

Combination Products – Multiple Classes *(continued)*		
doravirine/lamivudine/ tenofovir disoproxil fumarate (Delstrigo®), *DOR/3TC/TDF*[45]	Merck	A co-formulated product containing 1 NNRTI and 2 NRTIs indicated as a complete regimen for the treatment of HIV-1 infection in adults and pediatric patients weighing ≥ 35 kg with no prior antiretroviral treatment history or to replace the current antiretroviral regimen in those who are virologically suppressed (HIV-1 RNA < 50 copies/mL) on a stable antiretroviral regimen with no history of treatment failure and no known substitutions associated with resistance to Delstrigo
efavirenz/emtricitabine/ tenofovir disoproxil fumarate (Atripla®), EFV/FTC/*TDF*[46‡]	generic, Gilead	A co-formulated product containing 2 NRTIs and 1 NNRTI used alone as a complete regimen or in combination with other antiretroviral agents for the treatment of HIV-1 infection in adults and pediatric patients weighing ≥ 40 kg
efavirenz/lamivudine/ tenofovir disoproxil fumarate (Syfy®), *EFV/3TC/TDF*[47]	Laurus, Mylan	A co-formulated product containing 1 NNRTI and 2 NRTIs indicated as a complete regimen for the treatment of HIV-1 infection in adult and pediatric patients weighing ≥ 40 kg
efavirenz/lamivudine/ tenofovir disoproxil fumarate (Symfi Lo®), *EFV/3TC/TDF*[48]	Laurus, Mylan	A co-formulated product containing 1 NNRTI and 2 NRTIs indicated as a complete regimen for the treatment of HIV-1 infection in adults and pediatric patients weighing ≥ 35 kg

HIV - AIDS

Combination Products – Multiple Classes *(continued)*		
elvitegravir/cobicistat/ emtricitabine/tenofovir alafenamide (TAF) (Genvoya®), *EVG/c/FTC/TAF*[50]	Gilead	A co-formulated product containing 1 INSTI, 1 pharmacokinetic enhancer, and 2 NRTIs for the treatment of HIV-1 infection in adults and pediatric patients weighing ≥ 25 kg who have no antiretroviral treatment history or to replace the current antiretroviral regimen in those who are virologically suppressed (HIV-1 RNA < 50 copies/mL) on a stable antiretroviral regimen for ≥ 6 months with no history of treatment failure and no known substitutions associated with resistance to its components
elvitegravir/cobicistat/ emtricitabine/tenofovir disoproxil fumarate (Stribild®), *EVG/c/FTC/TDF*[51]	Gilead	A co-formulated product containing 1 INSTI, 1 pharmacokinetic enhancer, and 2 NRTIs as a complete regimen for the treatment of HIV-1 infection in adults and pediatric patients ≥ 12 years old and weighing ≥ 35 kg who are antiretroviral treatment-naïve or to replace the current antiretroviral regimen in those who are virologically suppressed (HIV-1 RNA < 50 copies/mL) on a stable antiretroviral regimen for ≥ 6 months with no history of treatment failure and no known substitutions associated with resistance to the individual components

HIV - AIDS

Drug	Manufacturer	Indication(s)
Combination Products – Multiple Classes *(continued)*		
emtricitabine/rilpivirine/ tenofovir alafenamide (Odefsey®), *FTC/RPV/TAF*[51]	Gilead	A combination product containing 2 NRTIs and 1 NNRTI indicated for the treatment of HIV-1 infection in patients ≥ 35 kg as initial therapy in treatment-naïve patients with HIV-1 RNA ≤ 100,000 copies/mL or to replace a stable antiretroviral regimen in those who are virologically suppressed (HIV-1 RNA < 50 copies/mL) for ≥ 6 months with no history of treatment failure and no known substitutions associated with resistance to the individual components
rilpivirine/emtricitabine/ tenofovir disoproxil fumarate (Complera®), *RPV/FTC/TDF*[52]	Gilead	A co-formulated product containing 2 NRTIs and 1 NNRTI used as a complete regimen for the treatment of HIV-1 infection in treatment-naïve patients ≥ 12 years old and weighing ≥ 35 kg with HIV-1 RNA ≤ 100,000 copies/mL at the start of therapy; As an alternate regimen for the treatment of HIV-1 infection in certain adult patients who are virologically suppressed (HIV-1 RNA < 50 copies/mL) on a stable ritonavir-boosted PI regimen at start of therapy in order to replace their current antiretroviral treatment regimen

HIV - AIDS

- It is estimated that there were approximately 38.4 million people living with HIV by the end of 2021
- Of new infections, approximately 66% are from male-to-male sexual contact, 23% from heterosexual contact, and 7% from injection drug use
- Newly infected HIV patients dropped from 3.4 million to 1.7 million from 1996 to 2019, as well as a decline in the number of children acquiring HIV by 52% from 2010 to 2019
- In 2020, The Joint United Nations Programme on HIV/AIDS UNAIDS intensified their targets for 2025

HIV - AIDS

- Goals include the 95-95-95 treatment target: 95% of people living with HIV are aware of their status, 95% of these patients are receiving treatment, and 95% of them have achieved viral suppression
- Additionally, they seek to achieve 95% of women have access to HIV and sexual and reproductive health services, 95% of coverage services to eliminate vertical transmission, and 95% use of combination prevention
- Prevention of maternal-fetal HIV transmission has also continued to improve worldwide
- All guidelines advise initiating antiretroviral therapy regardless of CD4 cell counts in HIV-infected individuals who are prepared to commit to the regimen

HIV - AIDS

- Viral suppression requires multidrug therapy involving 2 or more antiretroviral subclasses
- There are several established regimens that are successful when used in the appropriate stage of a patient's HIV infection
- All currently recommended treatment regimens for treatment-naïve individuals utilize drugs from the following classes:
  - nucleos(t)ide reverse transcriptase inhibitors (NRTIs)
  - non-nucleoside reverse transcriptase inhibitors (NNRTIs)
  - protease inhibitors (PIs)
  - integrase strand transfer inhibitors (INSTIs)

HIV - AIDS

- INSTI-based regimens are now considered first-line therapy for treatment-naïve patients in current guidelines
- NNRTI-based regimens have a low threshold for the development of resistance
- PI-based regimens have more virologic potency and durability, as well as higher barriers to resistance compared to other regimens
- However, PIs have more concerning adverse event profiles
- CCR5-based regimens are also effective but require expensive coreceptor tropism assays prior to use and need more studies with other NRTIs
- In patients who are experiencing treatment failure, HIV RNA genotypic drug-resistance testing and next generation sequencing genotypic resistance assays are available

HIV - AIDS

- Sunlenca, monoclonal antibody, ibalizumab-uiyk (Trogarzo), and an attachment inhibitor, fostemsavir (Rukobia), are indicated in heavily treatment-experienced adults with multidrug resistant HIV-1 infection who are failing their current antiretroviral regimens
- For Individuals at high risk to contract HIV, pre-exposure pharmacologic prophylaxis (PrEP) includes emtricitabine/tenofovir disoproxil fumarate (Truvada) and emtricitabine/tenofovir alafenamide (Descovy), cabotegravir (Vocabria; short-term use), and cabotegravir extended-release (Apretude)

HIV - AIDS

Clinical and Product Updates

- CDC Communication (April 2024):
  - CDC issued a Health Alert Network (HAN) Health Advisory to alert Healthcare Practitioners to an increase in invasive meningococcal disease, mainly attributable to Neisseria meningitidis serogroup Y
  - In 2023, 422 cases were reported in the US, an annual high number since 2014
  - As of March 25, 2024, there has been an increase by 62% (143 cases) for the current calendar year
  - Cases caused by this strain are disproportionately occurring in people ages 30–60 years (65%), Black or African American people (63%), and people with HIV (15%)
  - In addition, most cases of invasive meningococcal disease caused by ST-1466 in 2023 had a clinical presentation other than meningitis
  - Healthcare providers should 1) have a heightened suspicion for meningococcal disease, particularly among populations disproportionately affected by the current increase, 2) be aware that patients may present without symptoms typical of meningitis

Leukotriene Modifiers

Leukotriene Modifiers

Class Overview:

- montelukast - (montelukast chewable tablet, granules & tablet; Singulair Chewable Tablet, Granules & Tablet)
- zafirlukast - (Accolate; zafirlukast)
- zileuton- (zileuton ER; Zyflo; Zyflo CR)

Leukotriene Modifiers

- Zafirlukast, zileuton, and zileuton ER are only approved for prophylaxis and chronic treatment of asthma
- Montelukast is the only leukotriene modifier that is approved for asthma and allergic rhinitis and can be considered for patients with these two co-morbidities
- National Asthma Education and Prevention Program (NAEPP) and Global Initiative for Asthma (GINA) guidelines recommend inhaled corticosteroids (ICS) as the cornerstone for the treatment of asthma
- Leukotriene modifiers are included as potential alternatives or add-on therapy in some patients
- GINA states that leukotriene modifiers are less effective than ICS, but may be appropriate for initial controller treatment for patients unable or unwilling to use ICS, intolerant to ICS, or who also have allergic rhinitis

Leukotriene Modifiers

- Leukotriene modifiers are also used as add-on therapy to reduce the dose of the ICS in patients with moderate to severe asthma, and to potentially improve asthma control in patients whose asthma is not controlled with low or high doses of ICS
- Limited data exist to support the use of leukotriene modifiers in acute asthma
- The American Academy of Allergy, Asthma and Immunology (AAAAI), the American College of Allergy, Asthma, and Immunology (ACAAI), and the American Academy of Otolaryngology, Head and Neck Surgery recommend intranasal corticosteroids (INCS) as first line treatment for patients with seasonal allergic rhinitis (SAR)
- Montelukast is considered an alternative to first-line therapy with INCS in patients who suffer from both asthma and SAR

Leukotriene Modifiers

- The International Consensus Statement on Allergy and Rhinology Allergic Rhinitis guidelines state that leukotriene receptor antagonist monotherapy can be a useful alternative in patients with contraindications for INCSs and oral antihistamines
- Currently, high-quality comparative trials of the leukotriene modifiers are limited
- Montelukast is the most widely used leukotriene modifier because of its multiple indications, once daily dosing, and ease of administration due to several different dosage forms

Movement Disorder Agents

Movement Disorders

FDA-Approved Indications

Drug	Manufacturer	Indication(s)
deutetrabenazine (Austedo®, Austedo® XR*)[1]	Teva	Treatment of chorea associated with Huntington's disease Treatment of tardive dyskinesia
tetrabenazine (Xenazine®)[2]	generic, Lundbeck	Treatment of chorea associated with Huntington's disease
valbenazine (Ingrezza®, Ingrezza® Sprinkle)[3]	Neurocrine Biosciences	Treatment of chorea associated with Huntington's disease Treatment of tardive dyskinesia

*Deutetrabenazine extended-release (Austedo XR) was approved under a 505(b)(2) regulatory pathway where reports of investigations of safety and effectiveness were provided, but at least some of the information required for approval may come from studies not conducted by or for the applicant[4,5]

Movement Disorders

- There are various types of movement disorders, including parkinsonism, tremor, dystonia, dyskinesia, tics, chorea, and other involuntary movements
- Chorea is a characteristic feature of Huntington's disease (HD)
- It affects approximately 90% of people with HD (over 35,000 people in the US)
- The 2012 American Academy of Neurology (AAN) guidelines, that were retired in 2022, recommend tetrabenazine, amantadine, or riluzole for chorea associated with HD
- Austedo has not been addressed in these clinical practice guidelines; however, an update to the guidelines is in progress
- Austedo and tetrabenazine have both demonstrated superiority over placebo but have not been compared head-to-head in controlled trials

Movement Disorders

- Both tetrabenazine and Austedo carry a boxed warning for depression and suicidality
- Tardive dyskinesia (TD) consists of involuntary movements of the tongue, lips, face, trunk, and extremities
- TD generally occurs after long-term treatment with dopamine antagonists
- It occurs at a rate of approximately 4% to 8% per year in adult patients treated with a first-generation antipsychotics, which appears to be about 3 times the rate that has been observed with second-generation antipsychotics
- In 2020, the American Psychiatric Association (APA) updated their guidelines for the treatment of schizophrenia
- They recommend that patients who have moderate to severe or disabling TD related to antipsychotic therapy be treated with Austedo, tetrabenazine, or Ingrezza (1B)

Movement Disorders

- They state that Austedo or Ingrezza is preferred over tetrabenazine due to the data supporting their use
- Patients with mild TD can also be considered for treatment with a VMAT2 inhibitor following an assessment of several factors
- Ingrezza and Austedo have demonstrated superiority over placebo in key clinical trials, but they have not been compared to each other or to other treatment strategies for TD

Movement Disorders

- The International Parkinson and Movement Disorder Society (MDS) commissioned an evidence-based review on treatments for Huntington's disease, and results were published in early 2022
  - Using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach, the group appraised 22 randomized controlled trials of 17 interventions targeting several predetermined questions
  - High quality data were limited. Relevant to pharmacotherapeutic treatments in this class, the group found that both deutetrabenazine and tetrabenazine are likely efficacious for chorea
  - They also concluded that deutetrabenazine is likely efficacious for motor impairment, while tetrabenazine is unlikely efficacious

Movement Disorders

- MDS evidence-based review continued:
  - Similarly, deutetrabenazine is likely efficacious for dystonia, but data were too limited regarding tetrabenazine
  - Deutetrabenazine and tetrabenazine were determined unlikely efficacious in functional capacity improvement as well as gait and balance. Notably, both agents are only approved for the treatment of chorea associated with Huntington's disease
  - Regarding safety of interventions, the group categorized deutetrabenazine as unlikely harmful while tetrabenazine was considered likely harmful

Movement Disorders

Clinical and Product Updates

- The FDA has approved Ingrezza Sprinkle (valbenazine) capsules for patients who have dysphagia or difficulty swallowing
- Ingrezza Sprinkle will be available as 40 mg, 60 mg, & 80 mg capsules that contain oral granules that can be sprinkled onto soft food
- The capsule contents should not be mixed with milk or water and should not be administered via enteral tubes

Movement Disorders

Clinical and Product Updates

- The FDA has approved Austedo XR (deutetrabenazine) new intermediate strength (18 mg) ER tablets
- A new 4-week titration kit has also been approved which contains seven 12 mg ER tabs, seven 18 mg ER tabs, seven 24 mg ER tabs, & seven 30 mg ER tabs

Phosphate Binders

Phosphate Binders

Drug	Manufacturer	Indication(s)
calcium acetate*[1]	generic	To reduce serum phosphorus in adult with end stage renal disease (ESRD)
calcium acetate†[2]	generic	For the reduction of serum phosphorus in adult with ESRD
calcium acetate (Phoslyra®)‡[3]	Fresenius Medical Care	To reduce serum phosphorus in adult with ESRD
ferric citrate (Auryxia®)[4]	Keryx Biopharmaceuticals	For the control of serum phosphorus levels in adults with chronic kidney disease (CKD) on dialysis Treatment of iron deficiency anemia in adults with CKD not on dialysis
lanthanum carbonate (Fosrenol®)[5]	generic, Shire	To reduce serum phosphate in adults with ESRD
sevelamer carbonate (Renvela®)[6]	generic, Genzyme	Control of serum phosphorus in patients ≥ 6 years of age with CKD on dialysis
sevelamer hydrochloride (Renagel®)[7]	generic, Genzyme	For the control of serum phosphorus in adults with CKD on dialysis
sucroferric oxyhydroxide (Velphoro®)[8]	Fresenius Medical Care	For the control of serum phosphorus in adults with CKD on dialysis

* Generic for PhosLo® tablets by Fresenius Medical Care. Previously, another equivalent generic product was available under the trade name Eliphos® by Hawthorn. Both the PhosLo tablet and Eliphos products have been discontinued.

† Generic for PhosLo® gelcaps/capsules by Fresenius Medical Care; the brand has been discontinued.

‡ Fresenius Medical Care has discontinued Phoslyra as of April 5, 2023; product may remain until supply has been depleted.[9]

Phosphate Binders

- Chronic kidney disease (CKD) affects approximately 37 million Americans in the United States (US)
- As kidney function deteriorates, the ability to eliminate phosphorus declines, resulting in hyperphosphatemia, one of the complications of CKD
- Elevated levels of phosphorus inhibit the conversion of 24-hydroxyvitamin D to 1,25-dihydroxyvitamin D (calcitriol)
- The reduction in calcitriol decreases intestinal absorption of calcium and eventually leads to hypocalcemia

Phosphate Binders

- In end stage renal disease (ESRD), patients are at risk for several complications of hyperphosphatemia, including the development of renal bone disease and extraosseous calcifications of soft tissue and vasculature
- Hyperphosphatemia (> 6.5 mg/dL) is also associated with increased risk of death
- All phosphate binders are considered effective in reducing serum phosphate levels, and treatment guidelines do not strongly prefer one agent in this class over another for adults

Phosphate Binders

- The National Kidney Foundation (NKF) 2017 Clinical Practice Guideline for the Diagnosis, Evaluation, Prevention, and Treatment of Chronic Kidney Disease – Mineral and Bone Disorder (CKD-MBD) under The Kidney Disease: Improving Global Outcomes (KDIGO) foundation advise that treatment of hyperphosphatemia includes the reduction of dietary phosphorus, phosphate binding therapy, and removal of phosphorus by dialysis and should consider serial phosphate, calcium, and PTH levels
- Although the recommendation is not graded, they advise basing decisions regarding phosphate-lowering treatment on progressively or persistently elevated serum phosphate rather than to prevent hyperphosphatemia

Sedative Hypnotics

Sedative Hypnotics

Class Overview: Benzodiazepine Agents

- estazolam - (estazolam)
- flurazepam - (flurazepam)
- quazepam – (Doral; quazepam)
- temazepam - (Restoril; temazepam)
- triazolam - (Halcion; triazolam)

Sedative Hypnotics

Class Overview: Non-Benzodiazepine Agents

- daridorexant (Quviviq)
- doxepin - (doxepin; Silenor)
- eszopiclone - (eszopiclone; Lunesta)
- lemborexant - (Dayvigo)
- ramelteon - (ramelteon; Rozerem)
- suvorexant - (Belsomra)
- tasimelteon - (tasimelteon, Hetlioz capsule; Hetlioz LQ)
- zaleplon - (Sonata; zaleplon)
- zolpidem - (Ambien; Ambien CR; Edluar; Intermezzo; zolpidem tablet; zolpidem capsule, zolpidem SL; zolpidem ER; Zolpimist)

Sedative Hypnotics

- Insomnia is a symptom complex that comprises difficulties falling asleep, staying asleep, or non-refreshing sleep, in combination with daytime dysfunction or distress
- It is estimated that about 10% to 15% of people have chronic insomnia
- Insomnia affects up to 30% of children and the prevalence of sleep disorders is as high as 80% in those with special needs
- Non-pharmacological measures should be used first to treat insomnia
- The 2017 American Academy of Sleep Medicine (AASM) guidelines recommend psychological and behavioral strategies, as well as pharmacological interventions
- The guidelines recommend that initial behavioral interventions should include stimulus control or relaxation therapy, or a combination of therapies referred to as cognitive behavioral therapy (CBT) for insomnia

Sedative Hypnotics

- AASM guidelines recommend that pharmacotherapy should be used to treat patients who failed to respond to CBT
- AASM recommends:
  - Zaleplon, triazolam, and ramelteon versus no treatment for sleep onset insomnia
  - Suvorexant and doxepin over no treatment for sleep maintenance insomnia
  - Eszopiclone, zolpidem, and temazepam for both sleep onset and sleep maintenance insomnia
  - Against the use of trazodone or tiagabine for sleep onset or for sleep maintenance insomnia in adults
  - Against the use of OTC medications, supplements, or herbal products as a treatment for sleep onset or sleep maintenance for chronic insomnia

Sedative Hypnotics

- Current treatment guidelines for insomnia do not recommend one agent within this class over another, suggesting treatment be individualized
- Choice of agent should be based on:
  - Symptom pattern
  - Treatment goals
  - Past treatment response
  - Patient preference
  - Cost
  - Availability of other treatment options
  - Comorbid conditions
  - Contraindications
  - Potential interactions with concurrent medications
  - Adverse effects

Sedative Hypnotics

- Non-24-hour sleep-wake disorder (N24SWD or non-24) is a chronic circadian rhythm disorder that causes problems with the timing of sleep and sleep patterns
- Tasimelteon capsule (Hetlioz) is approved for non-24 in totally blind adults and for nighttime sleep disturbances in Smith-Magenis Syndrome (SMS) in patients ≥ 16 years of age
- Newly approved tasimelteon oral suspension (Hetlioz LQ) is indicated for nighttime sleep disturbances in SMS in pediatric patients 3 years to 15 years of age only
- Tasimelteon capsules (Hetlioz) and oral suspension (Hetlioz LQ) are not interchangeable

Sedative Hypnotics

- Except for zolpidem SL, all agents should be administered immediately before going to bed or after the patient has gone to bed and experienced difficulty falling asleep
- Zolpidem SL should be utilized for middle of the night awakenings when the patient still has more than 4 hours before planned waking time
- Due to gender differences in zolpidem clearance, women generally require lower doses of zolpidem
- Doxepin, ramelteon, and tasimelteon are the only agents in this class that are not controlled substances
- All drugs in this class should be used at the lowest effective dose
- All sedative/hypnotics should be administered with caution in patients exhibiting signs and symptoms of depression

Sedative Hypnotics

- Patients whose insomnia fails to remit after 7 to 10 days of treatment may need to be evaluated for other medical or psychological issues
- Continuous use should be avoided; patients should be encouraged to use these medications only when necessary
- Concurrent use of opioids and benzodiazepines or other CNS depressants may result in serious adverse reactions such as profound sedation, respiratory depression, coma, and death
- Providers should limit prescribing opioids with benzodiazepines to only patients without alternative treatment options
- The benzodiazepines carry boxed warnings for the risk of abuse, misuse, addiction, dependence, and withdrawal
- A gradual taper to discontinue or reduce the dose is required to prevent acute withdrawal symptoms which could be fatal

Steroids, Topical

Steroids, Topical

Class Overview: Low Potency Topical Steroid Products

- alclometasone dipropionate – (alclometasone dipropionate cream & ointment)
- desonide – (Desonate Gel; Desowen Cream; desonide cream, lotion & ointment; Tridesilon; Verdeso)
- fluocinolone acetonide – (Capex Shampoo; Dema-Smoothe-FS; fluocinolone 0.01% oil)
- fluocinolone acetonide/Cetaphil cleanser lotion (Xilapak Kit)
- fluocinolone acetonide/ urea* (NoxiPak Kit)

Steroids, Topical

Class Overview: Low Potency Topical Steroid Products

- hydrocortisone (Advanced Allergy Collection Kit, Ala-Cort, Ala-Scalp, Aquanil, Anti-Itch, Aqua Glycolic HC Kit, Beta HC, Cortaid, Cortisone, Cortizone, Dermarest Eczema, Dermasorb HC Complete Kit, GS Anti-Itch, MiCort HC, Noble Formula HC, QC Anti-Itch, Scalacort, Scalacort-DK Kit, Scalp Relief, Scalpicin, Soothing Care, Texacort, Vanicream; hydrocortisone)
- hydrocortisone/aloe vera (Cortisone-10, Cortisone Plus Aloe, Nucort, QC Anti-Itch with Aloe, SM Hydrocortisone-Aloe, SM Hydrocortisone Plus; hydrocortisone/aloe vera)

Steroids, Topical

Class Overview: Medium Potency Topical Steroid Products

- betamethasone valerate - (betamethasone valerate foam; Luxiq)
- clocortolone pivalate - (clocortolone cream (AG); Cloderm)
- fluocinolone acetonide - (fluocinolone acetonide cream, ointment & solution; Synalar Ointment & Solution)
- flurandrenolide - (Cordran Tape; flurandrenolide cream, lotion, (AG) & ointment; Nolix)
- fluticasone propionate - (Cutivate Cream & Lotion; fluticasone cream, lotion & ointment)

Steroids, Topical

Class Overview: Medium Potency Topical Steroid Products

- hydrocortisone butyrate - (hydrocortisone butyrate cream, cream (AG), lotion, ointment, ointment (AG), solution & solution (AG); Locoid / Lipocream)
- hydrocortisone probutate - (Pandel)
- hydrocortisone valerate - (hydrocortisone valerate cream & ointment)
- mometasone furoate - (Elocon Cream & Ointment; mometasone furoate cream, ointment & solution)
- prednicarbate - (Dermatop; prednicarbate cream & ointment)

Steroids, Topical

Class Overview: High Potency Topical Steroid Products

- amcinonide - (amcinonide cream & lotion)
- betamethasone dipropionate - (betamethasone dipropionate cream, gel, lotion & ointment; Sernivo Spray)
- betamethasone valerate - (betamethasone valerate cream & ointment)
- betamethasone dipropionate augmented cream (Diprolene AF)
- desoximetasone - (desoximetasone cream, gel & ointment; Topicort Ointment & Spray)
- diflorasone diacetate - (diflorasone diacetate cream & ointment)
- fluocinonide - (fluocinonide cream, gel, ointment & solution; Vanos)

Steroids, Topical

Class Overview: High Potency Topical Steroid Products

- fluocinonide/emollient - (fluocinonide emollient)
- halcinonide - (Halog Cream & Ointment)
- triamcinolone acetonide/dimethicone - (Ellzia Pak)
- triamcinolone acetonide/silicones - (DermacinRx Silazone; Silazone-II)
- triamcinolone acetonide - (Kenalog Aerosol; triamcinolone acetonide aerosol, cream, lotion & ointment; Trianex Ointment)
- triamcinolone acetonide/dimethicone/silicones - (DermacinRx Silapak; triamcinolone acetonide/dimethicone)
- triamcinolone/emollient - (Dermasorb TA)

Steroids, Topical

Class Overview: Very High Potency Topical Steroid Products

- clobetasol propionate - (Impeklo)
- clobetasol propionate - (clobetasol lotion; clobetasol propionate cream, gel, ointment, solution, spray & spray (AG); clobetasol shampoo; Clobex Lotion, Shampoo & Spray; Olux; Temovate Cream)
- clobetasol propionate/clobetasol propionate/emollient - (clobetasol propionate foam)
- clobetasol propionate/emollient - (clobetasol propionate/emollient)
- clobetasol propionate/skin cleanser - (Clodan Kit)
- diflorasone diacetate/emollient - (Apexicon E)

Steroids, Topical

Class Overview: Very High Potency Topical Steroid Products

- halobetasol propionate - (halobetasol propionate cream & ointment; Ultravate Lotion)
- halobetasol/lactic acid - (Ultravate X Pac Cream & Ointment)
- Halobetasol propionate foam - (Lexette)
- halobetasol propionate lotion - (Bryhali)

Steroids, Topical

- Topical corticosteroids are used in a variety of inflammatory skin conditions
- Atopic dermatitis (AD) is a chronic, inflammatory dermatologic condition and is often referred to as “eczema”
- AD commonly occurs in patients affected by asthma and/or allergic rhinitis and is associated with elevated serum IgE levels
- AD can present at any age, but prevails most frequently in children
- Psoriasis is another inflammatory skin condition, with plaque psoriasis being the most common type frequently forming on the elbows, knees, lower back, and scalp
- Alternating the use of topical corticosteroids with non-corticosteroids or steroid-sparing agents (e.g., vitamin D analogs, tazarotene, calcineurin inhibitors) is also recommended as a means of mitigating the potential side effects of topical corticosteroids

Steroids, Topical

- Seborrheic dermatitis is an inflammatory disorder affecting areas of the head and trunk, where sebaceous glands are most prominent
- Pharmacotherapy choices for these conditions include emollients and topical corticosteroids
- Emollients remain the cornerstone of any AD treatment regimen
- Topical corticosteroids are the standard of care to which other treatments are compared
- The selection of medication and potency should depend on:
  - Medication efficacy
  - Severity of disease
  - Location and surface area of affected skin
  - Intended duration of treatment

Steroids, Topical

  - Medication vehicle
  - Patient preference
  - Patient age
- In short-term durations of treatment, high potency medications have greater efficacy when compared to less potent medications, but with an increased risk in side effects
- Increased incidences of adverse dermatologic reactions are positively correlated with the medication's frequency and duration of use
- True efficacy and risk of long-term topical corticosteroid use is unknown because most clinical trials only involved short-term studies

Steroids, Topical

- Treatment guidelines from the American Academy of Dermatology recommend that continued therapy be supervised and a gradual reduction in utilization is appropriate once a clinical response is demonstrated
- There are differing compendia listings for corticosteroid potencies
- Efficacy of topical corticosteroids is relative to their potency, but individual agents within a potency category are not distinguishable from each other

New Drug Reviews

Umang Patel, Pharm.D.

AHCCCS
Arizona Health Care Cost Containment System

New Products

- Agamree (vamorolone)
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- Rezdiffra (Resmetirom)
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- Wainua (Eplontersen)
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Agamree (vamorolone)

- Agamree (vamorolone), a corticosteroid, for the treatment of patients ≥ 2 years of age with Duchenne muscular dystrophy (DMD)
- Recommended dosage is 6 mg/kg orally once daily (max 300 mg for pts weighing > 50kg)
  - Some pts may respond to 2 mg/kg/d dose
- Available as a 40 mg/mL oral suspension
- The most common adverse reactions are cushingoid features, psychiatric disorders, vomiting, weight increased, and vitamin D deficiency.
- Warnings include:
  - Alterations in Endocrine Function
  - Immunosuppression and Increased Risk of Infection
  - Alterations in Cardiovascular/Renal Function

Agamree (vamorolone)

- The efficacy of vamorolone for the treatment of DMD was evaluated in a phase 2b, multicenter, randomized, double-blind, parallel-group, placebo- and active controlled, multinational 24-week study.
- The study randomized 121 male patients with DMD to one of the following treatment groups: vamorolone 6 mg/kg/day (n=30), 2 mg/kg/day (n=30), prednisone 0.75 mg/kg/day (n=31), or placebo (n=30) for 24 weeks (Period 1).
- After 24 weeks, patients on prednisone and placebo received either vamorolone 6 mg/kg/day (n=29) or 2 mg/kg/day (n=29) for an additional 24 weeks (Period 2).
- Primary Endpoint: Change from baseline to Week 24 in Time to Stand Test (TTSTAND) velocity for vamorolone 6 mg/kg/day vs. placebo

Agamree (vamorolone)

- Secondary Endpoints: Change from baseline to Week 24 in the following measures, using a fixed sequential testing process in the order listed below.
  - TTSTAND velocity (vamorolone 2 mg/kg/day vs. placebo)
  - 6 Minute Walk Test (6MWT) distance (vamorolone 6 mg/kg/day vs. placebo and 2 mg/kg/day vs. placebo)
  - The 6MWT measures the distance that a patient can walk on a flat, hard surface in a period of 6 minutes.
  - Time to Run/Walk 10 meters (TTRW) velocity (vamorolone 6 mg/kg/day vs. placebo and 2 mg/kg/day vs. placebo).
  - The TTRW measures the time that it takes a patient to run or walk 10 meters.
- The primary endpoint and key secondary endpoints were met for the vamorolone 6 mg/kg/day treatment group.
- The 2 mg/kg/day treatment group was statistically significant vs. placebo for TTSTAND and 6MWT, but was not statistically significant vs. placebo for TTRW.
- Relative efficacy of prednisone and vamorolone, 6 mg/kg per day, were similar for these motor outcomes.
- Vamorolone, 2 mg/kg per day, showed similar effectiveness as prednisone for TTSTAND and 6MWT but less effectiveness for TTRW.

Fabhalta (iptacopan)

- Fabhalta is a complement factor B inhibitor, indicated for the treatment of adults with paroxysmal nocturnal hemoglobinuria (PNH).
- It is available as a 200 mg capsule.
- Dosing is 200 mg orally twice daily with or without food.
- Contains a BBW for its increase in risk of serious or life-threatening infections caused by encapsulated bacteria including *Step. pneumoniae, Neisseria meningitidis,* and *Haemophilus influenzae type B.*
- Most common adverse reactions in adults with PNH were headache, nasopharyngitis, diarrhea, abdominal pain, bacterial infection, viral infection, nausea and rash.
- Warnings and precautions include hyperlipidemia.

Fabhalta (iptacopan)

- **APPLY-PNH (NCT04558918; ongoing, unpublished)**: An open-label, active-controlled, phase 3 clinical trial evaluated the use of iptacopan in adult patients with PNH and residual anemia (hemoglobin <10 g/dL) on anti-C5 treatment (eculizumab or ravulizumab).
- Patients were required to have been on a stable regimen of the anti-C5 product for >6 months before participation in the trial.
- A total of 97 patients were randomized 8:5 to change to treatment with iptacopan (200 mg orally twice daily; n=62) or to continue anti-C5 treatment (US- and non-US-approved eculizumab, n=23; US- and non-US-approved ravulizumab, n=12) for 24 weeks.
- The primary endpoints, assessed after 24 weeks of treatment, evaluated the proportion of patients demonstrating a hematological response, defined as:
  - 1) Sustained increase in hemoglobin of >2 g/dL from baseline in the absence of red blood cell (RBC) transfusions; and
  - 2) Sustained hemoglobin level >12 g/dL in the absence of RBC transfusions.

Fabhalta (iptacopan)

- Results showed:
  - 82% of patients in treatment arm had a sustained increase in hemoglobin of >2 g/dL from baseline in the absence of RBC transfusion compared to 0% in the placebo arm (p value <0.0001)
  - 67% of patients in the treatment arm had a sustained hemoglobin level >12 g/dL in the absence of RBC compared to 0% in the placebo arm (p value < 0.0001)

Litfulo (ritlecitinib)

- A kinase inhibitor indicated for the treatment of severe alopecia areata in adults and adolescents 12 years and older.
  - Limitations of Use: Not recommended for use in combination with other JAK inhibitors, biologic immunomodulators, cyclosporine or other potent immunosuppressants
- Recommended dosage is 50 mg orally once daily
- Available as 50 mg capsules
- Most common adverse reactions are headache, diarrhea, acne, rash, urticaria, folliculitis, pyrexia, atopic dermatitis, dizziness, blood creatine phosphokinase increased, herpes zoster, red blood cell count decreased, and stomatitis.
- Contains a BBW for serious infections, mortality, malignancy, major adverse cardiovascular events (MACE), and thrombosis

Litfulo (ritlecitinib)

- Efficacy and safety of ritlecitinib were evaluated in one phase 2b-3, randomized, double-blind, placebo-controlled trial in subjects age >12 years with AA and >50% scalp hair loss, including alopecia totalis (AT) and alopecia universalis (AU).
- Trial AA-I evaluated a total of 718 subjects who were randomized to one of the following treatment regimens for 48 weeks:
  - 1) 200 mg once daily for 4 weeks followed by 50 mg once daily for 44 weeks
  - 2) 200 mg once daily for 4 weeks followed by 30 mg once daily for 44 weeks
  - 3) 50 mg once daily for 48 weeks
  - 4) 30 mg once daily for 48 weeks
  - 5) 10 mg once daily for 48 weeks
  - 6) placebo for 24 weeks followed by 200 mg once daily for 4 weeks and 50 mg once daily for 20 weeks
  - 7) placebo for 24 weeks followed by 50 mg once daily for 24 weeks
- Ritlecitinib was evaluated vs. placebo for 24 weeks (the randomized control period), followed by a 24-week extension period during which ritlecitinib groups continued their assigned doses and patients initially assigned to placebo switched to ritlecitinib.

Litfulo (ritlecitinib)

- Primary Endpoint: The primary endpoint was response based on SALT score <20 (<20% scalp hair loss) at week 24, defined as a clinically meaningful treatment outcome by both clinicians and patients.
- Secondary Endpoints: The key secondary endpoint was response based on SALT score <10 (<10% scalp hair loss) at week 24. Other secondary endpoints included PGI-C score of moderately improved or greatly improved; responses to week 48; eyebrow and eyelash regrowth.
- Results: At Week 24, a greater proportion of subjects had a SALT <20 response (<20% of scalp hair loss) and SALT <10 response (<10% of scalp hair loss) with ritlecitinib 50 mg vs. placebo.
    - Ritlecitinib 50 mg once daily (n=130) vs. placebo (n=131) [percent responders]
        - Proportion of subjects with response on the SALT scale at week 24: (1,5)
        - SALT <20 response (scalp hair loss <20%): ritlecitinib 23.0%; placebo 1.6%; difference vs. placebo 21.4%, 95% CI (13.4, 29.5)
        - SALT <10 response (scalp hair loss <10%); ritlecitinib 13.4%; placebo 1.5%; difference vs.placebo 11.9%, 95% CI (5.4, 18.3)
        - Response rates continued to increase up to week 48 (end of study).

Litfulo (ritlecitinib)

- Results: (Cont'd)
  - PGI-C response (moderately improved/greatly improved) at week 24:
    - ritlecitinib 49.17%; placebo 9.23%; difference vs. placebo 39.96%, 95% CI (28.85, 51.06)
    - Response rates continued to increase beyond week 24 up to week 48.
  - Eyebrow/eyelash regrowth: Among patients without normal eyebrow assessment or eyelash assessment scores at baseline, eyebrow and eyelash responses (>2 grade improvement from baseline in eyebrow assessment score or a normal score in eyelash assessment score) increased over time with ritlecitinib.

Rezdiffra (Resmetirom)

- Resmetirom (Rezdiffra) is a thyroid hormone receptor-beta (THR-beta) agonist approved by the FDA in conjunction with diet & exercise for treatment of adults with noncirrhotic nonalcoholic steatohepatitis (NASH) with moderate to advanced liver fibrosis (consistent with stages F2 to F3 fibrosis).
- Rezdiffra is the first medication for NASH, also known as metabolic dysfunction-associated steatohepatitis (MASH), to be approved by the FDA.
- Approved under Accelerated Approval based on improvement of NASH & fibrosis; continued approval may be contingent upon verification & description of clinical benefit in confirmatory trials.
- Rezdiffra should be avoided in pts with decompensated cirrhosis.
- Recommended dosage is 80 mg orally once daily for pts weighing < 100 kg & 100 mg orally once daily for pts weighing ≥ 100 kg (based on actual body weight).
- Product will be available as 60 mg, 80 mg, & 100 mg tablets.

Rezdiffra (Resmetirom)

- There are no contraindications.
- Resmetirom carries a warning for hepatotoxicity.
- Resmetirom has a warning for Gallbladder-Related Adverse Reactions (Cholelithiasis and cholecystitis were observed more often in patients with resmetirom-treated patients)
- Most Common Adverse Reactions:
    - Diarrhea
    - Nausea
    - Pruritus
    - Vomiting
    - Constipation
    - Abdominal Pain
    - Dizziness

Rezdiffra (Resmetirom)

- The efficacy of resmetirom were evaluated at Month 12 in a Phase 3 trial (NCT03900429) that included a 54-month, double-blind, randomized, placebo-controlled trial (n=966).
- Enrolled patients had metabolic risk factors and a baseline or recent liver biopsy showing NASH with fibrosis stage 2 or 3 and a NAFLD Activity Score (NAS) of at least 4.
- Efficacy determination was based on the effect of REZDIFFRA on resolution of steatohepatitis without worsening of fibrosis and one stage improvement in fibrosis without worsening of steatohepatitis, on post-baseline liver biopsies collected at 12 months
- The month 12 analysis included 888 F2 and F3 (at eligibility) patients randomized 1:1:1 to receive placebo (n = 294), REZDIFFRA 80 mg once daily (n = 298), or REZDIFFRA 100 mg once daily (n = 296), in addition to lifestyle counseling on nutrition and exercise. Patients were on stable doses of medications for diabetes, dyslipidemia, and hypertension.

Rezdiffra (Resmetirom)

- NASH resolution with no worsening of fibrosis was achieved in 25.9% of the patients in the 80-mg resmetirom group and 29.9% of those in the 100-mg resmetirom group, as compared with 9.7% of those in the placebo group (P<0.001 for both comparisons with placebo).
- Fibrosis improvement by at least one stage with no worsening of the NAFLD activity score was achieved in 24.2% of the patients in the 80-mg resmetirom group and 25.9% of those in the 100-mg resmetirom group, as compared with 14.2% of those in the placebo group (P<0.001 for both comparisons with placebo).
- The change in low-density lipoprotein cholesterol levels from baseline to week 24 was -13.6% in the 80-mg resmetirom group and -16.3% in the 100-mg resmetirom group, as compared with 0.1% in the placebo group (P<0.001 for both comparisons with placebo).

Rivfloza (Nedosiran)

- Indicated to lower urinary oxalate levels in children ≥ 9 years old and adults with primary hyperoxaluria type 1 (PH1) and relatively preserved kidney function, e.g., eGFR ≥30 mL/min/1.73 m2
- Dosage ranges from 3.3 mg/kg once monthly to 160 mg subcutaneously once monthly based on age and weight
- Available as:
  - 80 mg (0.5 mL) single-dose Vial
  - 128 mg (0.8 mL) single-dose Pre-filled Syringe
  - 160 mg (1 mL) single-dose Pre-filled Syringe
- No contraindications or warnings
- Adverse reactions include injection site reactions

Rivfloza (Nedosiran)

- PHYOX2 was a phase 2 clinical trial and interim data from the ongoing phase 3 PHYOX3 extension study
- PHYOX2 met its primary endpoint, showing that patients treated with Rivfloza achieved a marked reduction from baseline in 24 hour-urinary oxalate (Uox) excretion from Day 90 to Day 180
- The percent change from baseline in 24-hour Uox was measured using an area under the curve (AUC) analysis
- The least-squares (LS) mean between group difference of AUC24-hour Uox was 4976, which was significant between the Rivfloza and placebo groups over the 90 days
- Interim results from the PHYOX3 extension study showed reductions in 24-hour Uox excretion were maintained in the 13 patients with PH1 who had received an additional six months of treatment with Rivfloza

Spevigo (Spesolimab)

- Indicated for the treatment of generalized pustular psoriasis (GPP) in adults and pediatric patients ≥ 12 years old and weighing at least 40 kg
- **Subcutaneous Dosage for Treatment of GPP When Not Experiencing a Flare**
  - Administer a subcutaneous loading dose of 600 mg (four 150 mg injections), followed by 300 mg (two 150 mg injections) subcutaneously 4 weeks later and every 4 weeks thereafter
- **Subcutaneous Use After Intravenous Spevigo for Treatment of GPP Flare**
  - Four weeks after treatment with intravenous Spevigo, initiate or reinitiate subcutaneous Spevigo at a dose of 300 mg (two 150 mg injections) administered every 4 weeks

Spevigo (Spesolimab)

- **Intravenous Dosage for Treatment of GPP Flare**
  - Administer as a single 900 mg dose by intravenous infusion over 90 minutes
  - If flare symptoms persist, may administer an additional intravenous 900 mg dose one week after the initial dose
- For subcutaneous use
  - Available as 150 mg/mL solution in a single-dose prefilled syringe
- For intravenous use
  - Available as 450 mg/7.5 mL (60 mg/mL) solution in a single-dose vial
- Contraindicated in patients with severe or life-threatening hypersensitivity to Spevigo or to any of the excipients in Spevigo

Spevigo (Spesolimab)

- Warnings
  - Infections
  - Risk of Tuberculosis (TB)
  - Hypersensitivity and Infusion-Related Reactions
  - Vaccinations
- Adverse Reactions
  - **Treatment of GPP When Not Experiencing a Flare**: injection site reaction, urinary tract infection, arthralgia, and pruritus
  - **Treatment of GPP Flare**: asthenia and fatigue, nausea and vomiting, headache, pruritus and prurigo, infusion site hematoma and bruising, and urinary tract infection

Spevigo (Spesolimab)

- EFFISAYIL 1 was a 12-week phase 2 clinical trial
- Patients (n=53) experiencing a GPP flare were treated with a single 900 mg intravenous dose of Spevigo or placebo
- The majority of patients at the outset of the trial had a high, or very high, density of pustules, and impaired quality of life
- After one week, 54% of patients treated with Spevigo showed no visible pustules compared to 6% of patients treated with placebo
- Approval in pediatric patients aged 12 years and older weighing ≥40 kg. was based on the results of the EFFISAYIL 2 clinical trial
- The 48-week study showed that Spevigo significantly reduced the risk of GPP flares by 84%, compared with placebo
- In the trial (n=123), no flares were observed after week 4 of Spevigo subcutaneous treatment in the high-dose group (n=30)

Voydeya (danicopan)

- Indicated as add-on therapy to ravulizumab or eculizumab for the treatment of extravascular hemolysis (EVH) in adult patients with paroxysmal nocturnal hemoglobinuria (PNH)
  - Limitations of use: Danicopan has not been shown to be effective as monotherapy and should only be prescribed in combination with ravulizumab or eculizumab
- The recommended initial dose of danicopan is 150 mg orally three times daily, with or without food
- The dose may be increased to 200 mg three times daily:
  - If hemoglobin has not increased by >2 g/dL after 4 weeks of therapy
  - If the patient required a transfusion in the past 4 weeks of treatment
  - To achieve an appropriate hemoglobin response based on clinical judgement
- Available as 50 mg and 100 mg tablets
- Adverse reactions: headaches, vomiting, and pyrexia

Voydeya (danicopan)

- An exploratory, first-in-patient, open-label, phase 2 clinical trial evaluated the use of danicopan monotherapy in patients with PNH
- Eligible patients were adults with untreated PNH, a hemoglobin <12 g/dL, and a LDH >1.5 times the upper limit of normal (ULN)
- A total of 10 patients received danicopan at a starting dose of 100 or 150 mg three times daily; dose escalation up to 200 mg three times daily was permitted at the investigator's discretion
- The primary efficacy endpoint was change in LDH from baseline at day 28. Secondary efficacy parameters included change in hemoglobin at days 28 and 84, and change in LDH from baseline to day 84

Voydeya (danicopan)

- Primary endpoint:
  - A significant reduction in LDH was observed over the 28-day treatment period in all 10 patients
  - At baseline, the mean LDH value was 5.7 ± 2.17 times the ULN, which was reduced to a mean value of 1.8 ± 1.03 times the ULN at day 28 ($p<0.001$)
  - The percentages of patients with LDH values <3 times, <2 times, and <1 time the ULN were 90%, 60%, and 40%, respectively

- Secondary endpoints:
  - Mean hemoglobin values increased with danicopan treatment, from 9.8 g/dL at baseline to 10.9 g/dL at day 28, 10.9 g/dL at day 56, and 11.5 g/dL at day 84 (all $p<0.005$)
  - LDH reductions were maintained through day 84, with a value of 2.3 ± 1.41 the ULN at day 56 ($p<0.005$) and 2.2 ± 1.04 the ULN at day 84 ($p<0.001$)

Voydeya (danicopan)

Study ACH471-101 (NCT03472885; published):

- An exploratory, open-label, phase 2 clinical trial evaluated the addition of danicopan in patients with PNH and an inadequate response to eculizumab therapy
- Eligible patients were adults with a confirmed diagnosis of PNH and RBC transfusion-dependent anemia (>1 RBC transfusion within 12 weeks prior to screening)
- A total of 12 patients received danicopan in addition to eculizumab for 24 weeks
- Danicopan was initiated at a dose of 100 or 150 mg three times daily; dose escalation up to 200 mg three times daily was permitted based on hemoglobin values and assessment of patient safety
- The primary endpoint was change in hemoglobin from baseline to week 24; secondary endpoints measured reduction in RBC transfusions, percentage of patients demonstrating transfusion independence, and LDH levels at week 24

Voydeya (danicopan)

Study ACH471-101 (NCT03472885; published):

- Efficacy analyses were conducted in 11 patients. Median age, 48 years old; mean LDH at baseline, 244.5 IU/L; mean hemoglobin at baseline, 7.9 g/dL
- Primary endpoint:
  - There was a significant increase in hemoglobin at week 24 (10.3 g/dL; increase from baseline, 2.4 g/dL; p=0.0001)
- Secondary endpoints:
  - A clinically meaningful reduction in RBC transfusion was noted with danicopan treatment
  - After treatment was initiated, only 1 patient received a single RBC transfusion, which occurred during a hospitalization for pneumonia and was considered unlikely to be related to danicopan by the investigators
  - LDH levels did not change over the 24-week treatment period

Wainua (Eplontersen)

- Indicated for the treatment of the polyneuropathy of hereditary transthyretin-mediated amyloidosis in adults
- Dosage is 45 mg administered by subcutaneous injection once monthly
- Available as 45 mg/0.8 mL injection in a single-dose autoinjector
- Warning
  - Reduced Serum Vitamin A Levels and Recommended Supplementation
- Adverse reactions
  - Decrease in vitamin A
  - Vomiting

Wainua (Eplontersen)

- The NEURO-TTRansform Phase 3 trial was a 35-week interim analysis
- The trial enrolled adult patients with ATTRv-PN Stage 1 or Stage 2 compared to the external placebo group from the Teggsedi (inotersen) NEURO-TTR registrational trial that Ionis completed in 2017
- The comparison of efficacy and safety for Wainua versus external placebo was based on data up to week 66
- All patients were followed on treatment until week 85, when they had the option to transition into an open-label extension study
- In the trial, patients treated with Wainua demonstrated consistent and sustained benefit on the three co-primary endpoints

Wainua (Eplontersen)

- These include serum transthyretin (TTR) concentration, neuropathy impairment measured by modified Neuropathy Impairment Score +7 (mNIS+7) and quality of life (QoL) on the Norfolk Quality of Life Questionnaire-Diabetic Neuropathy (Norfolk QoL-DN)
- Wainua achieved a least squares (LS) mean reduction of 82% in TTR serum concentration from baseline at 65 weeks, compared to an 11% reduction from baseline in the external placebo group
- Wainua demonstrated statistically significant benefits on both mNIS+7 and Norfolk QoL-DN at 35 weeks versus the external placebo group
- At week 66, Wainua halted disease progression by mNIS+7, resulting in a 0.3 point LS mean increase compared to a 25.1 point increase for the external placebo group from baseline

Wainua (Eplontersen)

- Overall, 47% of treated patients showed improvements in neuropathy at 66 weeks compared to baseline versus 17% in the external placebo group.
- Among study completers, 53% of treated patients showed improvements in neuropathy at 66 weeks compared to baseline versus 19% in the external placebo group.
- Wainua improved QoL demonstrating a 5.5 point LS mean decrease at 66 weeks (improvement), compared to a 14.2 point increase (worsening) in the external placebo group
- 58% of treated patients showed improvements in QoL at 66 weeks compared to baseline versus 20% in the external placebo group
- Among study completers, 65% of treated patients showed improvements in QoL at 66 weeks compared to baseline versus 23% in the external placebo group

Zilbrysq (Zilucoplan)

- Indicated for the treatment of generalized myasthenia gravis (gMG) in adult patients who are anti-acetylcholine receptor (AChR) antibody positive
- Patients should be vaccinated for meningococcal infection at least 2 weeks prior to administering the first dose of Zilbrysq
- Prior to treatment initiation, baseline lipase and amylase levels should be obtained
- Given once daily as a subcutaneous injection; dosage is dependent on actual body weight and ranges from 16.6 mg to 32.4 mg
- Available as 16.6 mg/0.416 mL, 23 mg/0.574 mL, or 32.4 mg/0.81 mL injections in single-dose prefilled syringes
- Contraindicated in patients with unresolved Neisseria meningitidis infection

Zilbrysq (Zilucoplan)

- Boxed Warning:
  - Serious Meningococcal Infections
- Healthcare providers who prescribe Zilbrysq must enroll in the Zilbrysq REMS
- Additional Warnings:
  - Other Infections
  - Pancreatitis and Pancreatic Cysts
- Adverse reactions include injection site reactions, upper respiratory tract infection, and diarrhea

Zilbrysq (Zilucoplan)

- The RAISE study was a multi-center, Phase 3, randomized, double-blind, placebo-controlled study
- The trial assessed the efficacy, safety profile, and tolerability of Zilbrysq in adult patients with AChR antibody-positive gMG
- Patients were randomized in a 1:1 ratio to receive daily subcutaneous injections of 0.3 mg/kg Zilbrysq or placebo for 12 weeks
- The primary endpoint was change from baseline to Week 12 in the Myasthenia Gravis-Activities of Daily Living (MG-ADL) score
- The MG-ADL is an eight-item patient-reported outcome measure assessing MG symptoms and functional activities related to activities of daily living

Zilbrysq (Zilucoplan)

- Each of the items is scored, from 0 (normal) to 3 (most severe), providing a total MG-ADL score ranging from 0 to 24, where higher scores indicate greater severity of symptoms
- As a secondary endpoint, the efficacy of Zilbrysq was also measured using the Quantitative Myasthenia Gravis (QMG) total score which is a 13-item categorical grading system that assesses muscle weakness
- Each item is assessed on a 4-point scale where a score of 0 represents no weakness and a score of 3 represents severe weakness
- Total possible score ranges from 0 to 39, where higher scores indicate more severe impairment

Zilbrysq (Zilucoplan)

- At week 12, treatment with Zilbrysq demonstrated a statistically significant improvement from baseline compared to placebo for MG-ADL total score and QMG total score
- Other secondary endpoints included the proportion of patients with improvements of at least 3 and 5 points in the MG-ADL total score and QMG total score, respectively, at Week 12 without rescue therapy



Break and Executive Session

Public Therapeutic Class Votes

Biosimilar Update

Meeting Adjournment

Future Meeting Date: January 29, 2025