





AHCCCS Pharmacy and Therapeutics Committee

October 18, 2021

AHCCCS
Arizona Health Care Cost Containment System

Welcome and Introductions

- Suzi Berman, RPh, AHCCCS Pharmacy Director
  - May 19, 2021 - P&T Minutes Review and Vote
  - All submitted written testimony will be posted on the AHCCCS website under Pharmacy/Pharmacy & Therapeutics Committee

Magellan Class Reviews

Classes for Review: Non-Supplemental Rebate Class Review

- Antimigraine Agents, Triptans
- Leukotriene Modifiers
- Sedative Hypnotics
- Topical Steroids – Low, Medium, High & Very High Potency
- Antifungals, Oral
- Antifungals, Topical

Magellan Class Reviews

Classes for Review: Non-Supplemental Rebate Class Review

- Beta Blockers
- BPH Treatments
- Calcium Channel Blockers
- HIV/AIDS
- Movement Disorders

Magellan Class Reviews

Classes for Review: Supplemental Rebate Class Review

- Continuous Glucose Monitors (CGM)




Magellan Drug Class Reviews

Hind Douiki, Pharm.D.

Antimigraine Agents, Triptans

Antimigraine Agents, Triptans

Class Overview:

- almotriptan malate - (almotriptan)
- eletriptan - (eletriptan; Relpax)
- frovatriptan - (frovatriptan; Frova)
- naratriptan - (Amerge; 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)

Antimigraine Agents, Triptans

Class Overview:

- sumatriptan/naproxen - (sumatriptan/naproxen; Treximet)
- sumatriptan camphor/menthol - (Migranow)
- zolmitriptan - (zolmitriptan ODT, ODT (AG), tablets, tablets (AG); Zomig, ZMT)

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
    - Frovatriptan is established for short-term menstrually-associated migraine (MAM) prevention
    - Naratriptan, zolmitriptan, antidepressants (amitriptyline, venlafaxine), and beta-blockers (atenolol, nadolol) are considered *probably effective* in migraine 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

Product/Guideline Updates:

- In 2021, the AHS released an updated position statement on integrating new migraine treatments into clinical practice
- They state these agents may be considered in patients who have contraindications to, inability to tolerate, or have failed to respond to at least 2 oral triptans, as assessed by a validated questionnaire or clinician attestation
- Zomig (zolmitriptan) nasal spray is now available as a generic

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

Leukotriene Modifiers

Product Updates:

- None

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

- doxepin - (doxepin; Silenor)
- eszopiclone - (eszopiclone; Lunesta)
- lemborexant - (Dayvigo)
- ramelteon - (ramelteon; Rozerem)
- suvorexant - (Belsomra)
- tasimelteon - (Hetlioz capsule; Hetlioz LQ)
- zaleplon - (Sonata; zaleplon)
- zolpidem - (Ambien; Ambien CR; Edluar; Intermezzo; zolpidem; 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
- Non-pharmacological measures should be used first to treat insomnia
- The updated 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 guideline recommends 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 treatments 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
- With the exception of 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

Sedative Hypnotics

- 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
- Patients whose insomnia fails to remit after 7 to 10 days of treatment may need to be evaluated for other medical or psychological issues

Sedative Hypnotics

- 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

Sedative Hypnotics

Treatment Updates:

- None

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

Steroids, Topical

Product/Guideline Updates:

- FDA approved an expanded indication for halobetasol propionate foam for the topical treatment of plaque psoriasis to include patients as young as 12 years; previously only approved in adults

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)

Antifungals, Oral

Class Overview

- 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

Product Updates:

- The FDA has approved a new formulation of Noxafil, Noxafil Powdermix delayed-release oral suspension
- It is indicated for the prophylaxis of invasive Aspergillus and Candida infections in patients who are at high risk of developing these infections due to being severely immunocompromised, such as hematopoietic stem cell transplant (HSCT) recipients with graft-versus-host disease (GVHD) or those with hematologic malignancies with prolonged neutropenia from chemotherapy for pediatric patients ≥ 2 years of age (who weigh ≤40 kg)

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 8% - (Ciclodan Solution, ciclopirox 8%, Penlac)
- ciclopirox 8% / triamcinolone acetonide - (Trilociclo)
- clotrimazole - (Alevazol [OTC], clotrimazole [OTC], Lotrimin AF [OTC])
- clotrimazole/betamethasone - (clotrimazole/betamethasone, DermacinRx Therazole Pak, Lotrisone)
- econazole cream - (econazole)

Antifungals, Topical

Class Overview:

- econazole foam - (Ecoza)
- econazole / triamcinolone acetonide - (Triamazole)
- efinaconazole - (Jublia)
- ketoconazole - (Extina, ketoconazole, Nizoral A-D Shampoo, Nizoral Shampoo, Xolegel)
- luliconazole - (Luzu)
- miconazole - (Azolen [OTC], Desenex [OTC] , Fungoid [OTC], Lotrimin AF Spray, [OTC], miconazole [OTC], Zeasorb [OTC], Mycozyl AP [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], 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 with regard to prior treatments and complicating conditions, such as bacterial growth or intense inflammation

Antifungals, Topical

Product Updates:

- None

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)

Beta Blockers

Class Overview: Single Agents

- nadolol - (Corgard, nadolol)
- nebivolol - (Bystolic)
- pindolol - (pindolol)
- propranolol - (propranolol)
- propranolol - (Hemangeol)
- propranolol ER - (Inderal XL, Innopran XL)
- propranolol LA - (Inderal LA, propranolol LA)
- sotalol - (Betapace, sotalol)

Beta Blockers

Class Overview: Single Agents

- sotalol - (Betapace AF, sotalol AF)
- sotalol - (Sotylize)
- timolol - (timolol)

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)

Beta Blockers

Class Overview: Beta-Blocker/Diuretic Combinations

- nadolol/bendroflumethiazide - (Corzide, nadolol/bendroflumethiazide)
- propranolol/HCTZ - (propranolol/HCTZ)

Beta Blockers

- Approximately 116 million (47%) of adults in the United States have hypertension
- Highest prevalence is among African American adults and men at 56% and 50%, respectively
- It is estimated that hypertension is controlled in only 24% 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, HF, and diabetes

Beta Blockers

- Beta-blockers have similar efficacy for the treatment of hypertension (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)

Beta Blockers

Product Updates:

- The American Heart Association/American College of Cardiology (AHA/ACC) published guidelines on the diagnosis and treatment of hypertrophic cardiomyopathy (HCM)
- For symptomatic patients with left ventricular outflow tract (LVOT) obstruction, they recommend nonvasodilating beta-blockers, but alternatives for select patients include verapamil, diltiazem, or disopyramide
- For patients with nonobstructive HCM with preserved left ventricular ejection fraction (LVEF), beta-blockers, verapamil, or diltiazem are recommended
- Anticoagulants may be considered default therapeutic options for patients who also have atrial fibrillation independent of the CHA2DS2VASc score
- Additional guidance on the use of antiarrhythmic therapy and heart failure agents is included as well

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

- 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 American Urological Association (AUA) 2010 standards were reaffirmed in 2014
- They state patients with mild symptoms of BPH (AUA Symptom Score < 8) and patients with moderate or severe disease (AUA Symptom Score > 8) who are not bothered by their symptoms generally do not require pharmacologic intervention
- Alpha-adrenergic blocker therapy is an appropriate treatment option for patients with moderate to severe LUTS secondary to BPH
- The AUA indicates that alfuzosin, doxazosin, tamsulosin, and terazosin have equal clinical effectiveness
- However, selective alpha-blockers such as alfuzosin, tamsulosin, and silodosin may have a decreased incidence of hypotension-related adverse events

BPH Treatments

- Silodosin did not have published peer-reviewed studies prior to the guideline update
- Guidelines state the 5AR inhibitors are appropriate and effective treatments for patients with LUTS associated with demonstrable prostatic enlargement, but not for men with LUTS who do not have evidence of prostatic enlargement
- 5AR inhibitors may be used to prevent progression of LUTS secondary to BPH and to reduce the risk of urinary retention and future prostate-related surgery
- Combination therapy utilizing an alpha blocker and a 5α-reductase inhibitor is an appropriate and effective treatment for patients at highest risk for disease progression and for those who exhibit LUTS symptoms and have definitive prostatic enlargement

BPH Treatments

- The NIH-funded Medical Therapy of Prostatic Symptoms (MTOPS) and CombaT studies indicated that combination therapy is likely to be more effective at inhibiting disease progression than monotherapy
- 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

BPH Treatments

Product Updates:

- None

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)
- 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

Calcium Channel Blockers

Product/Guideline Updates:

- Pfizer will discontinue manufacturing Procardia 10 mg capsules and Procardia XL. Generic versions of Procardia remain available

HIV - AIDS

HIV - AIDS

Drug	Manufacturer	Indication(s)
Attachment Inhibitor		
fostemsavir (Rukobia™)	ViiV	Treatment of 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
CCR5 Antagonist		
maraviroc (Selzentry®), *MVC*	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*	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™)	ViiV	In combination with Edurant (rilpivirine) for short-term treatment of HIV-1 infection in adults 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: • Oral lead-in to assess the tolerability of cabotegravir prior to administration of Cabenuva (cabotegravir; rilpivirine) extended-release injectable suspensions • Oral therapy for patients who will miss planned injection dosing with Cabenuva
dolutegravir (Tivicay®, Tivicay PD®), *DTG*	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 components
raltegravir (Isentress®, Isentress HD®), *RAL*	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	Merck	In combination with other antiretroviral agents for the treatment of HIV-1 infection in adult patients 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	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	Janssen	In combination with other antiretroviral agents for the treatment of HIV-1 infection in treatment-experienced patients ≥ 2 years old

HIV - AIDS

Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs) (continued)		
nevirapine‡ (Viramune®), NVP	generic, Boehringer Ingelheim	In combination with other antiretroviral agents for the treatment of HIV-1 infection in adults and in pediatric patients ≥ 15 days old
nevirapine extended-release (Viramune® XR), NVP	generic, Boehringer Ingelheim	In combination with other antiretroviral agents for the treatment of HIV-1 infection in adults and in children ≥ 6 years of age with a BSA ≥ 1.17 m^2
rilpivirine (Edurant®), RPV	Janssen	In combination with other antiretroviral agents for the treatment of HIV-1 infection in treatment-naïve patients ≥ 12 years of age with HIV-1 RNA ≤ 100,000 copies/mL In combination with cabotegravir (Vocabria), for short-term treatment of HIV-1 infection in adults 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

HIV - AIDS

Nucleoside Reverse Transcriptase Inhibitors (NRTIs)		
abacavir (Ziagen®), *ABC*	generic, ViiV	In combination with other antiretroviral agents for the treatment of HIV-1 infection
didanosine (Videx®, Videx EC®), *ddI*	generic	In combination with other antiretroviral agents for the treatment of HIV-1 infection
emtricitabine (Emtriva®), *FTC*	Cipla, Gilead	In combination with other antiretroviral agents for the treatment of HIV-1 infection
lamivudine (Epivir®), *3TC*	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*	generic	In combination with other antiretroviral agents for the treatment of HIV-1 infection
zidovudine (Retrovir®), *AZT*	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*	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	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*	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*	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*	generic, ViiV	In combination with other antiretroviral agents for the treatment of HIV-1 infection
indinavir‖ (Crixivan®), *IDV*	Merck	In combination with other antiretroviral agents for the treatment of HIV-1 infection
nelfinavir (Viracept®), *NFV*	ViiV	In combination with other antiretroviral agents for the treatment of HIV-1 infection
ritonavir (Norvir®), *RTV* or *r*	generic, Abbvie	In combination with other antiretroviral agents for the treatment of HIV-1 infection
saquinavir (Invirase®), *SQV*	Genentech	Treatment of HIV-1 infection in combination with ritonavir and other antiretroviral agents in adults (≥ 16 years old)
tipranavir (Aptivus®±), *TPV*	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 protease inhibitor; not indicated for use in treatment-naïve patients

HIV - AIDS

Recombinant Monoclonal Antibody		
ibalizumab-uiyk (Trogarzo®)	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
Combination Products – Nucleos(t)ide Reverse Transcriptase Inhibitors (NRTIs)		
abacavir/lamivudine (Epzicom®), *ABC/3TC*	generic, ViiV	A co-formulated product containing 2 NRTIs used in combination with other antiretrovirals for the treatment of HIV-1 infection in adults and pediatric patients weighing ≥ 25 kg
abacavir/lamivudine/ zidovudine (Trizivir®), *ABC/3TC/AZT*	generic, ViiV	A co-formulated product containing 3 NRTIs used in combination with other antiretrovirals or alone for the treatment of HIV-1 infection in adults and pediatric patients weighing ≥ 40 kg

HIV - AIDS

Combination Products – Nucleos(t)ide Reverse Transcriptase Inhibitors (NRTIs) (continued)		
emtricitabine/tenofovir alafenamide (Descovy®), FTC/TAF	Gilead	A combination product containing 2 NRTIs used in combination with other antiretroviral agents for the treatment for HIV-1 infection in adults and pediatric patients weighing ≥ 35 kg or in combination with antiviral agents (other than protease inhibitors that require CYP3A inhibitors) for HIV-1 in pediatric patients weighing ≥ 25 kg to < 35 kg Indicated in at-risk adults and adolescents weighing ≥ 35 kg for pre-exposure prophylaxis (PrEP) to reduce the risk of HIV-1 infection from sexual acquisition, excluding individuals at risk from receptive vaginal sex; Individuals must have a negative HIV-1 test immediately prior to initiating for HIV-1 PrEP
emtricitabine/tenofovir disoproxil fumarate (Truvada®), FTC/TDF	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 pre-exposure prophylaxis (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

HIV - AIDS

Combination Products – Nucleos(t)ide Reverse Transcriptase Inhibitors (NRTIs) (continued)		
lamivudine/tenofovir disoproxil fumarate (Cimduo®), 3TC/TDF**	Mylan	A combination of 2 NRTIs indicated in combination with other antiretroviral agents for the treatment of HIV-1 infection in adult and pediatric patients weighing ≥ 35 kg
lamivudine/tenofovir disoproxil fumarate (Temixys™), 3TC/TDF	Celltrion	A combination of 2 NRTIs indicated in combination with other antiretroviral agents for the treatment of HIV-1 infection in adult and pediatric patients weighing ≥ 35 kg
lamivudine/zidovudine (Combivir®), 3TC/AZT	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	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	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	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	Gilead	A co-formulated product containing 1 INSTI and 2 NRTIs approved as a complete regimen for the treatment of HIV-1 infection in adults and pediatric patients weighing ≥ 25 kg who are antiretroviral-naive or who are virologically suppressed (HIV-1 RNA < 50 copies/mL) on their current, stable antiretroviral regimen for ≥ 3 months with no history of treatment failure and no known substitutions associated with resistance to its individual components
cabotegravir ER/rilpivirine ER (Cabenuva™)	ViiV	A co-packaged product containing an INSTI and 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 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	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

dolutegravir/abacavir/ lamivudine (Triumeq®), DTG/ABC/3TC	**ViiV**	**A co-formulated product containing 1 INSTI and 2 NRTIs indicated for the treatment of HIV-1 infection in adults and pediatric patients weighing ≥ 40 kg**
dolutegravir/lamivudine (Dovato®), DTG/3TC	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	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

doravirine/lamivudine/ tenofovir disoproxil fumarate (Delstrigo™), DOR/3TC/TDF	**Merck**	**A co-formulated product containing 1 NNRTI and 2 NRTIs indicated as a complete regimen for the treatment of HIV-1 infection in adult patients 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	Gilead, Teva	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 (Symfi®¥), EFV/3TC/TDF	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

HIV - AIDS

Combination Products – Multiple Classes (continued)		
efavirenz/lamivudine/ tenofovir disoproxil fumarate (Symfi Lo®), EFV/3TC/TDF	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 ≥ 35 kg
elvitegravir/cobicistat/ emtricitabine/tenofovir alafenamide (TAF) (Genvoya®), EVG/c/FTC/TAF	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	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

emtricitabine/rilpivirine/ tenofovir alafenamide (Odefsey®), FTC/RPV/TAF	**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	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 million people living with HIV by the end of 2020 , with 73% of adults and 54% of children receiving antiretroviral therapy (ART) globally
- 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
- 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

HIV - AIDS

- Prevention of maternal-fetal HIV transmission has also continued to improve worldwide due to the availability and improved utilization of antiretroviral therapy
- All guidelines advise initiating antiretroviral therapy regardless of CD4 cell counts in HIV-infected individuals who are prepared to commit to the regimen.
- 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

HIV - AIDS

- 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)
- 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

HIV - AIDS

- 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
- A 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

HIV - AIDS

- For Individuals at high risk to contract HIV, re-exposure pharmacologic prophylaxis (PrEP) includes emtricitabine/tenofovir disoproxil fumarate (Truvada) and emtricitabine/tenofovir alafenamide (Descovy)
- At this time, these are the only products that currently carry this indication

Movement Disorders

Movement Disorders

FDA-APPROVED INDICATIONS

Drug	Manufacturer	Indication(s)
deutetrabenazine (Austedo®)[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®)[3]	Neurocrine Biosciences	Treatment of tardive dyskinesia

Movement Disorders

- There are various types of movement disorders, including parkinsonism, tremor, dystonia, dyskinesia, tics, chorea, and other involuntary movements
- Chorea, an abnormal involuntary twisting or writhing movement, 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 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

Continuous Glucose Monitors

Continuous Glucose Monitors

Meter	Sensor/Transmitter	Sensor/Transmitter Size	Reader	Features	Calibration
Abbott Diabetes Care – Lifetime Warranty					
Freestyle Libre 14-Day	Indicated for patients 18 years and older; stays on body for up to 14 days; sensor must be manually scanned at least once every 8 hours; Glucose range: 40 - 500 mg/dL	1.38 in. diameter x 0.2 in; 0.18 oz; system does not involve use of a transmitter	Uses a portable reader instead of transmitter and receiver; readings are only captured when manually scanned with sensor; Reader dimensions: 2.36 in x 3.74 in x 0.63 in; weight: 2.3 oz	Water resistant in up to 3 ft of water for up to 30 minutes; Reader Memory: 90 days; Works with LibreView, a cloud-based diabetes-management system; FreeStyle Libre desktop software can be used to view reports and change reader settings; software is compatible with most Windows and Mac operating systems	None

Continuous Glucose Monitors

Dexcom – One-Year Warranty					
Dexcom G6	Indicated for patients aged ≥ 2 years; stays on body for up to 10 days; Sensor site location: ≥ 18 years of age – use abdomen 2 to 17 years of age – use abdomen or upper buttocks; Glucose range: 40 - 400 mg/dL	Reader must be kept within 20 feet of transmitter; Sensor and Transmitter: 1.8 in x 1.2 in x 0.6 in; weight: 0.42 oz	Readings automatically updated every 5 minutes; Size: 4.2 in x 2.5 in x 0.55 in; weight: 4 oz; Memory storage: 30 days of glucose data and 7 days of technical support data	Water resistant when submerged for up to 8 feet and up to 24 hours; can be used with a smart device by using an application (e.g., cell phone, smart watch) via Bluetooth; personalized alerts and alarms (e.g., hypoglycemia)	Optional – calibration is not required if users enter a sensor code; if users do not enter a sensor code daily fingerstick, calibration is required
Dexcom G5	Indicated for patients aged ≥ 2 years; stays on body for up to 7 days; Sensor site location: ≥ 18 years of age – use abdomen 2 to 17 years of age – use abdomen or upper buttocks; Glucose range: 40 - 400 mg/dL	Reader must be kept within 20 feet of transmitter; Sensor and Transmitter: 1.5 in x 0.9 in x 0.5 in; weight: 0.4 oz	Readings automatically updated every 5 minute; Size: 4 in x 1.8 in x 0.5 in; weight 2.4 oz; Memory storage: 30 days of glucose data and 7 days of technical support data	Water resistant when submerged for up to 8 feet and up to 24 hours; can be used with a smart device by using an application (e.g., cell phone, smart watch) via Bluetooth; personalized alerts and alarms (e.g., hypoglycemia)	Calibrated every 12 hours with finger sticks

Continuous Glucose Monitors

Meter	Sensor/Transmitter	Sensor/Transmitter Size	Reader	Features	Calibration
Dexcom – One-Year Warranty *(continued)*					
Dexcom G4 (PED)	Indicated for patients 2 to 17 years of age; stays on body for up to 7 days; place sensor on abdomen or upper buttocks; Glucose range: 40 - 400 mg/dL	Transmitter must be within 20 feet of reader; Sensor and Transmitter: 1.5 in x 0.9 in x 0.4-0.5 in (depending on device model); weight: 0.4 oz or 0.3 oz (depending on device model)	Readings automatically updated every 5 minutes; Size: 4 in x 1.8 in x 0.5 in; weight: 2.4 oz; Memory storage: 30 days of glucose data and 7 days of technical support data	Water resistant when submerged for up to 8 feet and up to 24 hours; can be used with a smart device by using an application (e.g., cell phone, smart watch) via Bluetooth; personalized alerts and alarms (e.g., hypoglycemia); Dexcom Share™ is an optional add on that allows remote viewing of the sensor, glucose readings, trends, and data by up to 5 other people	Calibrated every 12 hours with finger sticks
Dexcom G4	Indicated for patients ≥ 18 years of age; keep within 20 feet of display device; place sensor on abdomen; Glucose range: 40 - 400 mg/dL	Transmitter must be within 20 feet of reader; Sensor and Transmitter: 1.5 in x 0.9 in x 0.4-0.5 in (depending on device model); weight: 0.4 oz or 0.3 oz (depending on device model)	Readings automatically updated every 5 minutes; Size: 4 in x 1.8 in x 0.5 in; weight: 2.4 oz	Water resistant when submerged for up to 8 feet and up to 24 hours; can be used with a smart device by using an application (e.g., cell phone, smart watch) via Bluetooth; personalized alerts and alarms (e.g., hypoglycemia); Dexcom Share is an optional add on that allows remote viewing of the sensor, glucose readings, trends, and data by up to 5 other people	Calibrated every 12 hours with finger sticks

Continuous Glucose Monitors

- Continuous glucose monitoring (CGM) systems use a needle that remains inserted under the skin to measure glucose level within interstitial fluid
- Recent data support the use of a CGM, demonstrating both decreases in HbA1c and reduction in hypoglycemia frequency among users
- CGM provides data not previously available with traditional SMBG, including in new metrics, such as time in hypoglycemic range (TIR)
- There are CGM monitors that report glucose levels continuously, as well as those that require scanning the device to provide intermittent readings (intermittently scanning continuous glucose monitoring [isCGM])
- The latest version utilizing isCGM system has an optional alert for a high or low glucose value

Continuous Glucose Monitors

- This device (FreeStyle Libre 2) and one real-time CGM (rtCGM), the Dexcom G6, are considered to be integrated continuous glucose monitoring (iCGM) devices
- Patients should be evaluated by providers to determine readiness and if they are appropriate candidates prior to initiation of a CGM
- It is advised that blood glucose should be checked using a fingerstick reading, despite use of CGM, during the following situations:
  - To confirm hypoglycemia or impending hypoglycemia
  - When exhibiting symptoms of low or high blood glucose
  - When symptoms do not align with the CGM readings
  - During times of rapidly changing glucose

New Drug Reviews

Hind Douiki, Pharm.D.

AHCCCS
Arizona Health Care Cost Containment System

New Products

- Brexafemme (ibrexafungerp)
- Kloxxado (naloxone 8mg/0.1ml)
- Ponvory (ponesimod)
- Qelbree (viloxazine)

Brexafemme (ibrexafungerp)

- Indicated for the treatment of adult and post-menarchal pediatric females with vulvovaginal candidiasis
- dosage is 300 mg twice a day for one day
- Available as 150 mg tablets
- Contraindications include pregnancy and hypersensitivity to the active ingredient
- Carries a Risk of Fetal Toxicity warning
- Most frequent adverse reactions (≥ 2%):
  - Diarrhea
  - Dizziness
  - Vomiting
  - Abdominal pain
  - Nausea

Brexafemme (ibrexafungerp)

- Drug Interactions
  - Dose should be reduced with concomitant use of a strong CYP3A inhibitor to 150 mg twice daily for one day
  - Concomitant administration with strong or moderate CYP3A inducers should be avoided
- No comparative trials are available
- The FDA approval of Brexafemme was based on two Phase 3, randomized, double-blind, placebo-controlled, multi-center studies (VANISH-303 and VANISH-306)
- The trials were designed to evaluate the safety and efficacy of a single day of Brexafemme 600 mg (two 150 mg tablets per dose, administered 12 hours apart) for the treatment of VVC

Brexafemme (ibrexafungerp)

- The primary endpoint required for registration is clinical cure, defined as complete resolution (score of 0) of all signs and symptoms at the Day-10 test-of-cure (TOC) visit
- In VANISH-303 the observed clinical cure for Brexafemme was 50.5%, showing highly statistically significant superiority to placebo
- In VANISH-306, 63.3% of Brexafemme -treated patients met the primary endpoint of clinical cure at the Day-10 TOC visit

Kloxxado (naloxone)

- Indicated for the emergency treatment of known or suspected opioid overdose, as manifested by respiratory and/or central nervous system depression, for adult and pediatric patients
- Administered as a single spray to adult or pediatric patients intranasally into one nostril
- Emergency medical care should be sought immediately after use
- using a new nasal spray with each dose, additional doses may be administered if the patient does not respond or responds and then relapses into respiratory depression
- Additional doses may be given every 2 to 3 minutes until emergency medical assistance arrives
- Available as an 8 mg in 0.1 mL nasal spray

Kloxxado (naloxone)

Warnings:

- Risk of Recurrent Respiratory and CNS Depression
- Risk of Limited Efficacy with Partial Agonists or Mixed Agonist/Antagonists
- Precipitation of Severe Opioid Withdrawal
- Risk of Cardiovascular (CV) Effects

- Adverse reactions:
  - Abdominal pain
  - Nasal discomfort
  - Presyncope
  - Headache
  - Dizziness
  - Asthenia

Kloxxado (naloxone)

- Two pharmacokinetic studies were performed in a total of 47 healthy adult volunteers
- They were exposed to a single dose of Kloxxado, one spray in one nostril
- Each of the previously mentioned adverse reaction was reported in two subjects
- Signs of nasal inflammation and nasal congestion were also observed

Ponvory (Ponesimod)

- Indicated for the treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults
- Assessments and titration are both required prior to treatment initiation
- First-dose monitoring is recommended for patients with sinus bradycardia, first- or second-degree [Mobitz type I] atrioventricular (AV) block, or a history of myocardial infarction or heart failure
- The recommended maintenance dosage is 20 mg taken orally once daily
- Available as 2 mg, 3 mg, 4 mg, 5 mg, 6 mg, 7 mg, 8 mg, 9 mg, 10 mg, and 20 mg tablets

Ponvory (Ponesimod)

- Contraindications:
  - In the last 6 months, presence of myocardial infarction, unstable angina, stroke, transient ischemic attack (TIA), decompensated heart failure requiring hospitalization, or Class III/IV heart failure
  - Presence of Mobitz type II second-degree, third-degree AV block, or sick sinus syndrome, unless patient has a functioning pacemaker
- Warnings:
  - Infections
  - Liver Injury
  - Fetal Risk
  - Cutaneous Malignancies
  - Bradyarrhythmia and Atrioventricular Conduction Delays
  - Respiratory Effects
  - Increased Blood Pressure
  - Macular Edema

Ponvory (Ponesimod)

- Adverse reactions
  - Upper respiratory tract infection
  - Hepatic transaminase elevation
  - Hypertension
- Drug Interactions
  - Vaccines
  - Strong CYP3A4 and UGT1A1 inducers
- The FDA approval of Ponvory was based on the OPTIMUM (Oral Ponesimod Versus Teriflunomide In Relapsing Multiple Sclerosis) trial
- It was a head-to-head, prospective, multicenter, randomized, double-blind Phase 3 study that included 1,133 participants

Ponvory (Ponesimod)

- The clinical trial compared efficacy, safety and tolerability of Ponvory 20 mg versus teriflunomide (Aubagio) 14 mg in adults with relapsing MS
- The primary endpoint of the study was the annualized relapse rate (ARR) from baseline through the study period
- Ponvory 20 mg demonstrated superior efficacy in significantly reducing annual relapses by 30.5% compared to Aubagio 14 mg in patients with relapsing MS
- Over the study period, 71% of patients treated with Ponvory had no confirmed relapses, compared to 61% in the Aubagio group
- Ponvory was also superior to Aubagio in reducing the number of new gadolinium-enhancing (GdE) T1 lesions and the number of new or enlarging T2 lesions by 59% and 56%, respectively

Qelbree (viloxazine)

- Indicated for the treatment of Attention Deficit Hyperactivity Disorder (ADHD) in pediatric patients 6 to 17 years of age
- Recommended starting dosage for *patients 6 to 11 years of age* is 100 mg once daily; dose may be titrated in increments of 100 mg weekly to the maximum recommended dosage of 400 mg once daily
- Recommended starting dosage for *patients 12 to 17 years of age* is 200 mg once daily; dose may be titrated after 1 week, by an increment of 200mg, to the maximum recommended dosage of 400 mg once daily
- Available as 100 mg, 150 mg and 200 mg extended-release capsules

Qelbree (viloxazine)

- Contraindications:
  - Concomitant administration of monoamine oxidase inhibitors (MAOI), or dosing within 14 days after discontinuing an MAOI
  - Concomitant administration of sensitive CYP1A2 substrates or CYP1A2 substrates with a narrow therapeutic range
- Black Box Warning
  - Suicidal thoughts and behaviors
- Warnings
  - Blood Pressure and Heart Rate Increases
  - Activation of Mania or Hypomania
  - Somnolence and Fatigue

Qelbree (viloxazine)

- Adverse reactions:
  - Somnolence
  - Fatigue
  - Vomiting
  - Irritability
  - Decreased appetite
  - Nausea
  - Insomnia
- No comparative trials are available
- The FDA approval of Qelbree was based on three short-term, randomized, placebo-controlled monotherapy trials (Studies 1, 2, and 3)
- **Study 1** was a multicenter, randomized, double-blind, three-arm placebo-controlled, parallel group monotherapy trial in patients 6 to 11 years of age with ADHD

Qelbree (viloxazine)

- A total of 477 patients were randomized; 399 completed the study, and 78 discontinued
- The duration of the trial was 6 weeks, including a 1-week titration period (starting at 100 mg once daily) and a 5-week maintenance phase
- Patients were randomized to receive 100 mg, 200 mg, or placebo, given once daily as a single dose
- The primary endpoint was the change from baseline to the end of study on the total score on the ADHD Rating Scale (ADHD-RS-5)
- A key secondary endpoint was the Clinical Global Impression-Improvement (CGI-I) score at the end of the study
- Improvements in both ADHD-RS-5 total score and in CGI-I score were statistically significantly greater in patients treated with Qelbree 100 mg or 200 mg than in patients on placebo

Qelbree (viloxazine)

- **Study 2** was a multicenter, randomized, double-blind, three-arm, placebo-controlled, parallel group monotherapy trial in patients 6 to 11 years of age with ADHD
- A total of 313 patients were randomized (251 completed the study and 62 discontinued)
- The duration of treatment was 8 weeks, including a 3-week titration period (starting at 100 mg once daily), and a 5-week maintenance phase
- Patients were randomized to receive Qelbree 200 mg, Qelbree 400 mg, or placebo, given once daily as a single dose
- The primary endpoint was the change from baseline to the end of study on the total score on the ADHD-RS-5
- The CGI-I score at the end of the study was a secondary endpoint

Qelbree (viloxazine)

- Improvements in both ADHD-RS-5 total score and in CGI-I score were statistically significantly greater in patients treated with Qelbree 200 mg or 400 mg than in patients on placebo
- **Study 3** was a multicenter, randomized, double-blind, three-arm, placebo-controlled, parallel group monotherapy trial in patients 12 to 17 years of age with ADHD
- A total of 310 patients were randomized (266 completed and 44 discontinued)
- Total duration of treatment was 6 weeks, including 1-week titration period (starting at 200mg once daily) and a 5-week maintenance phase
- Patients were randomized to receive Qelbree 200 mg, Qelbree 400 mg, or placebo, given once daily as a single dose

Qelbree (viloxazine)

- The primary endpoint was the change from baseline to the end of study on the total score on the ADHD-RS-5
- The CGI-I score at the end of the study was a secondary endpoint
- Improvements in both ADHD-RS-5 total score and in CGI-I score were statistically significantly greater in patients treated with Qelbree 200 mg or 400 mg than in patients on placebo

P&T Requests

- Request by Dr. Kevin Chapman to allow Clonazepam ODT without PA for children < 6 years of age
- Request by Denise Volkov to remove prior authorization requirements for Budesonide inhalation vials



Executive Session

Public Therapeutic Class Votes

P&T Meeting Dates

- **Future Meeting Date:**
  - January 19, 2022