ARIZONA HEALTH CARE COST CONTAINMENT SYSTEM

# AHCCCS Pharmacy and Therapeutics Committee

October 22, 2025

# P&T Agenda

- Welcome and Introductions
- Minutes Review & Vote
- Non-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 May 21, 2025
  - Review
  - Vote

# Drug Class Reviews

## *Classes for Review: Non-Supplemental Rebate Classes*

- Analgesics Narcotics, Short Acting
- Angiotensin Modulators
- Angiotensin Modulator Combinations
- Anticonvulsants
- Antifungals, Oral
- Antifungals, Topical
- Antihistamines, Minimally Sedating
- Antimigraine Agents, Triptans
- Beta Blockers
- BPH Treatments
- Calcium Channel Blockers
- Contraceptives, Oral
- Contraceptives, Other
- Hypoglycemics, DPP4s
- Intranasal Rhinitis Agents
- Lipotropics, Statins
- Lipotropics, Other
- Ophthalmics, Glaucoma Agents
- Phosphate Binders
- Proton Pump Inhibitors

# Drug Class Reviews

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# Analgesics Narcotics, Short Acting

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# Analgesics Narcotics, Short Acting

| Drug | Federal Schedule | Manufacturer | Indication(s) |
|---|---|---|---|
| butorphanol nasal spray[1] | CIV | generic | Management of pain when the use of an opioid analgesic is appropriate |
| codeine sulfate[2] | CII | generic | Mild to moderately severe pain when use of an opioid analgesic is appropriate and for which alternative treatments are inadequate |
| codeine/acetaminophen[3] | CIII | generic | Mild to moderate pain |
| codeine/butalbital/ acetaminophen/caffeine (Fioricet® with codeine)[4] | CIII | generic, Actavis/Teva | Tension or muscle contraction headache |
| codeine/butalbital/aspirin/ caffeine (Ascomp with codeine)[5,6] | CIII | generic, Breckenridge | Tension or muscle contraction headache |
| codeine/carisoprodol/aspirin†[7] | CIII | Ingenus | Moderate pain and muscle spasm associated with acute, painful musculoskeletal conditions |
| dihydrocodeine bitartrate/ acetaminophen/caffeine (Trezix™)[8] | CIII | Xspire, Wraser | Moderate to moderately severe pain |
| fentanyl buccal (Fentora®)[9] | CII | Mayne*, Cephalon | Breakthrough cancer pain in patients with malignancies who are already receiving and who are tolerant to around-the-clock opioid therapy for their underlying persistent cancer pain |
| fentanyl transmucosal oral lozenge (Actiq®)[10] | CII | Mallinckrodt, Teva | Breakthrough cancer pain in patients with malignancies who are already receiving and who are tolerant to around-the-clock opioid therapy for their underlying persistent cancer pain |

# Analgesics Narcotics, Short Acting

| | | | |
|---|---|---|---|
| hydrocodone/acetaminophen solution (Lortab®)[11] | CII | generic, Akorn | Moderate to moderately severe pain |
| hydrocodone/acetaminophen tablet‡[12,13] | CII | generic | |
| hydrocodone/ibuprofen[14] | CII | generic | Short-term management of acute pain |
| hydromorphone (Dilaudid®)[15] | CII | generic, Rhodes | Management of pain in patients where an opioid analgesic is appropriate |
| levorphanol[16] | CII | generic | Moderate to severe pain |
| meperidine§[17,18] | CII | generic | Moderate to severe pain |
| morphine immediate release[19] | CII | generic | Moderate to severe acute and chronic pain |
| morphine immediate release‖[20,21] | CII | West-Ward/ Hikma, Roxane/ West-Ward | Moderate to severe acute pain in adults; Moderate to severe acute pain in pediatrics ≥ 2 years of age (oral solution) or weighing ≥ 50 kg (tablets) |
| oxycodone immediate release (Oxaydo®¶)[22] | CII | Egalet/Zyla | Moderate to severe acute and chronic pain |
| oxycodone immediate-release (Roxybond™)‖[23] | CII | Protega | Management of pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate |

# Analgesics Narcotics, Short Acting

***FDA-Approved Indications (continued)***

| Drug | Federal Schedule | Manufacturer | Indication(s) |
|---|---|---|---|
| oxycodone immediate release (Roxicodone®)[24,25] | CII | generic, Mallinckrodt | Moderate to severe pain in adults |
| oxycodone/acetaminophen (Endocet®, Nalocet®, Percocet®, Primlev™, Prolate®)[26,27,28,29,30] | CII | generic, Qualitest/Par, Forte Bio-Pharma, Endo, Akrimax, Forte Bio-Pharma | Moderate to severe pain |
| oxymorphone immediate release[31] | CII | generic | Moderate to severe acute pain |
| pentazocine/naloxone[32] | CIV | generic | Moderate to severe pain |
| tapentadol (Nucynta®)[33,34] | CII | Collegium | Acute pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate in adults and pediatric patients ≥ 6 years old with a body weight of ≥ 16 kg (solution only) and ≥ 40 kg (tablet) |
| tramadol[35,36] | CIV | generic | Management of moderate to moderately severe pain in adults |
| tramadol (Qdolo™)*‖[37] | CIV | generic, Athena | Management of pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate |
| tramadol/acetaminophen[38,39] | CIV | generic | Short-term (≤ 5 days) treatment of acute pain |
| tramadol/celecoxib (Seglentis®)‖[40] | CIV | Kowa | Management of acute pain in adults that is severe enough to require an opioid analgesic and for which alternative treatments are inadequate |

# Analgesics Narcotics, Short Acting

- Data from 2023 demonstrated that approximately 24.3% of adults report chronic pain in the U.S.
- Historically, data have suggested that pain may be undertreated, but newer estimates imply that opioid treatment for pain may be overutilized
- Nearly 80,000 (about 76%) of the 2023 overdose deaths involved opioids
- Inappropriate use of opioid analgesics is thought to have contributed to the national crisis of opioid-related morbidity, mortality, and misuse
- 2024 provisional data suggest that opioid-involved overdose death is projected to decrease by over 30%

# Analgesics Narcotics, Short Acting

- The World Health Organization's (WHO) guidelines for cancer pain management for adults recommend an approach with consideration for the type of pain and response to therapy
- If pain occurs, they recommend prompt oral administration of drugs in the following order:

  1. Non-opioids (acetaminophen, Non-Steroidal Anti-Inflammatory drugs [NSAIDs])
  2. As necessary, mild opioids (codeine)
  3. Strong opioids, until the patient is free of pain
- Per the American Society of Clinical Oncology (ASCO), opioids are recommended to be offered to patients with moderate to severe pain related to cancer or active treatment unless a contraindication is present

# Analgesics Narcotics, Short Acting

- NCCN guidelines recommend against the use of meperidine (due to CNS toxicity) and limited usefulness for cancer pain
- the Centers for Disease Control and Prevention (CDC) released guidelines for prescribing opioids for pain outside of sickle cell disease, cancer, palliative, and end-of-life care
- When opioid therapy is initiated for acute, subacute, or chronic pain, it should be started with immediate-release agents

# Analgesics Narcotics, Short Acting

- The American College of Physicians (ACP) and the American Academy of Family Physicians (AAFP) guidelines suggest against treating non-low back, musculoskeletal injury acute pain with opioids, including tramadol
- the North American Spine Society (NASS) published evidence-based clinical guidelines suggest that use of opioid pain medications for treating low back pain be limited and restricted to a short duration

# Analgesics Narcotics, Short Acting

- Per the ACP, opioids should only be considered in those who have failed the following therapies:

    1. Non-pharmacologic treatment
    2. An NSAID or skeletal muscle relaxant for acute or subacute low back pain
    3. NSAID as first-line pharmacologic therapy; tramadol or duloxetine as second-line therapy for chronic low back pain

- The American Society of Interventional Pain Physicians' (ASIPP) opioid prescribing guidelines for the management of patients with chronic, non-cancer pain recommend that all patients be screened for opioid abuse
- Also, providers should use urine drug testing and prescription drug monitoring programs to monitor for abuse

# Analgesics Narcotics, Short Acting

- The Institute for Clinical and Economic Review (ICER) published a final report on abuse-deterrent formulation (ADF) opioids
- At the time of evaluation, evidence showing a reduction in abuse risk with abuse-deterrent formulations compared to non-abuse-deterrent formulations risk was insufficient
- Roxybond (oxycodone) is the only immediate release opioid to have been FDA approved as an abuse-deterrent formulation

# Analgesics Narcotics, Short Acting

- Clinical guidelines do not recommend one opioid agent over another
- Pain management should be individualized, patient-centered, multimodal, and multidisciplinary
- Healthcare professionals and health systems should be aware of health inequities and provide appropriate communication and support for all persons
- All agents within this class are considered controlled substances
- They also contain a boxed warning regarding serious risks of misuse, abuse, addiction, overdose, and death as well as risks when combined with other central nervous system depressants

# Angiotensin Modulators

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# Angiotensin Modulators – ACE Inhibitors

| Drug | Manufacturer | HTN | CHF | Post-MI | Other Indications |
|---|---|---|---|---|---|
| ACE Inhibitors | | | | | |
| benazepril (Lotensin) | generic | X (Pediatrics age 6-16 yrs) | – | – | – |
| captopril (Capoten) | generic | X | X | X (in patients with LVD) | Diabetic Nephropathy in type 1 diabetes) |
| enalapril (Vasotec Epaned) | generic (tablets) Silvergate (oral solution) | X (Pediatrics age 1 month - 16 yrs) | X (or asymptomatic LVD) only tablets | – | – |
| fosinopril (Monopril) | generic | X (Pediatrics age 6-16 yrs) | X | – | – |
| lisinopril (Prinivil, Qbrelis, Zestril) | generic (tablets) Silvergate (oral solution) | X (Pediatrics age 6-16 yrs) | X | X (in hemodynamically stable patients) | – |
| moexipril (Univasc) | generic | X | – | – | – |

KEY: HTN = hypertension, LVD = left ventricular dysfunction, CAD = coronary artery disease, MI = myocardial infarction, CHF = congestive heart failure

# Angiotensin Modulators – ACE Inhibitors

| Drug | Manufacturer | HTN | CHF | Post-MI | Other Indications |
|---|---|---|---|---|---|
| ACE Inhibitors | | | | | |
| perindopril (Aceon) | genric | X | – | – | In stable CAD, reduces risk of cardiovascular mortality and non-fatal MI |
| quinapril (Accupril) | generic | X | X | – | – |
| ramipril (Altace) | generic (capsules) King (tablets) | X | X (post-MI) | – | Reduction of risk of MI, stroke, and death from cardiovascular causes |
| trandolapril (Mavik) | generic | X | X (post-MI) | – (in patients with CHF or LVD) | – |
| Renin Inhibitors | | | | | |
| aliskiren (Tektuma) | Novartis | X | – | – | – |

# Angiotensin Modulators – ACE Inhibitors

## *Diuretic Combination Products*

| Drug | Manufacturer |
|---|---|
| ACE Inhibitors | |
| benazepril/HCTZ (Lotensin HCT) | generic |
| captopril/HCTZ (Capozide) | generic |
| enalapril/HCTZ (Vaseretic) | generic |
| fosinopril/HCTZ | generic |
| lisinopril/HCTZ (Prinzide, Zestoretic) | generic |
| moexipril/HCTZ (Uniretic) | generic |
| quinapril/HCTZ (Accuretic) | generic |
| Renin Inhibitor | |
| aliskiren/HCTZ (Tekturna HCT) | Novartis |

# Angiotensin Modulators - ARBs

## FDA-Approved Indications

| Drug | Manufacturer | Indication(s) |
|---|---|---|
| **Angiotensin II Receptor Blockers: Single Agents** | | |
| azilsartan (Edarbi®) | Arbor/Azurity | ▪ Hypertension |
| candesartan (Atacand®) | generic, Ani | ▪ Hypertension (including ages 1 to < 17 years)<br>▪ Treatment of HF (LVEF ≤ 40%, NYHA II-IV) to reduce risk of CV death and reduce hospitalizations for HF (in addition to ACE inhibitors or when ACE inhibitors are not tolerated) |
| eprosartan | Mylan | ▪ Hypertension |
| irbesartan (Avapro®) | generic, Sanofi-Aventis | ▪ Hypertension<br>▪ Nephropathy in patients with type 2 diabetes |
| losartan (Cozaar®) | generic, Organon | ▪ Hypertension (including ages 6 to 16 years)<br>▪ Nephropathy in patients with type 2 diabetes<br>▪ Reduce the risk of stroke in hypertensive patients with LVH (not in African American patients) |
| losartan oral suspension (Arbli®) | Scienture | ▪ Hypertension (in adults and children > 6 years of age)<br>▪ Reduction of the risk of stroke in patients with hypertension and left ventricular hypertrophy<br>▪ Nephropathy with an elevated serum creatinine and proteinuria in patients with type 2 diabetes and history of hypertension |

# Angiotensin Modulators - ARBs

## FDA-Approved Indications (continued)

| Drug | Manufacturer | Indication(s) |
|---|---|---|
| **Angiotensin II Receptor Blockers: Single Agents** | | |
| olmesartan (Benicar®)[1] | generic, Cosette | ▪ Hypertension |
| telmisartan (Micardis®) | generic, Boehringer Ingelheim | ▪ Hypertension<br>▪ 80 mg tablets only: risk reduction of myocardial infarction (MI), stroke, or death from CV causes in patients ≥ 55 years at high risk of developing major CV events who are unable to take ACE inhibitors |
| valsartan (Diovan®) | generic, Novartis | ▪ Hypertension (in adults and children ≥ 1 year of age)<br>▪ Treatment of HF (NYHA II-IV) to reduce hospitalizations for HF<br>▪ Reduction of CV mortality in clinically stable patients with left ventricular failure or left ventricular dysfunction following MI |
| valsartan oral solution | Lifsa | ▪ Hypertension (in adults and children ≥ 6 years of age)<br>▪ Treatment of HF (NYHA II-IV) to reduce hospitalizations for HF in patients who are unable to swallow valsartan tablets<br>▪ Reduction of CV mortality in clinically stable patients with left ventricular failure or left ventricular dysfunction following MI who are unable to swallow valsartan tablets |

# Angiotensin Modulators - ARBs

## FDA-Approved Indications (continued)

| Drug | Manufacturer | Indication(s) |
|---|---|---|
| **Angiotensin II Receptor Blockers: Combination Products** | | |
| azilsartan/chlorthalidone (Edarbyclor®) | Arbor/Azurity | ▪ Hypertension (first-line therapy in patients requiring multiple agents) |
| candesartan/HCTZ (Atacand HCT®) | generic, Ani | ▪ Hypertension |
| irbesartan/HCTZ (Avalide®) | generic, Sanofi-Aventis | ▪ Hypertension (first-line therapy in patients requiring multiple agents) |
| losartan/HCTZ (Hyzaar®) | generic, Organon | ▪ Hypertension (first-line therapy in setting of prompt BP reduction)<br>▪ Reduce the risk of stroke in hypertensive patients with LVH (not in African American patients) |
| olmesartan/HCTZ (Benicar HCT®) | generic, Cosette | ▪ Hypertension |

# Angiotensin Modulators - ARBs

***FDA-Approved Indications (continued)***

| Drug | Manufacturer | Indication(s) |
|---|---|---|
| **Angiotensin II Receptor Blockers: Combination Products *(continued)*** | | |
| sacubitril/valsartan (Entresto®, Entresto® Sprinkle) | Novartis | ▪ Reduce the risk of CV death and hospitalization for HF in patients with chronic HF; its benefits are most clearly evident in patients with left ventricular ejection fraction (LVEF) below normal; clinical judgment is needed in deciding whom to treat<br>▪ Treatment of symptomatic HF with systemic left ventricular systolic dysfunction in pediatric patients ages ≥ 1 year |
| telmisartan/HCTZ (Micardis HCT®)[2] | generic, Boehringer Ingelheim | ▪ Hypertension |
| valsartan/HCTZ (Diovan HCT®) | generic, Novartis | ▪ Hypertension (first-line therapy in patients requiring multiple agents) |

ACE inhibitors = angiotensin converting enzyme inhibitors; CV = cardiovascular; HCTZ = hydrochlorothiazide; HF = heart failure; LVH = left ventricular hypertrophy; LVEF = left ventricular ejection fraction; NYHA = New York Heart Association Classification

# Angiotensin Modulators

- Approximately 120 million (48%) of adults in the U.S. 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)

# Angiotensin Modulators

- Per the JNC-8, in the non-African American population, initial treatment should include a thiazide-type diuretic, calcium channel blocker (CCB), angiotensin-converting enzyme (ACE) inhibitor, or ARB
- For African Americans, initial treatment should include a thiazide-type diuretic or CCB
- In patients with Chronic Kidney Disease (CKD), treatment should include an ACE inhibitor or ARB to improve kidney function

# Angiotensin Modulators

- If BP goal is not reached within 1 month of starting treatment, the dose should be increased or a second drug from another class should be added; a third drug can be added if needed
- According to the American College of Cardiology (ACC) and American Heart Association (AHA), first-line therapy recommendations for HTN include thiazide diuretics, CCBs, and ACE inhibitors or ARBs
- Patients with stage 2 hypertension (SBP ≥ 140 mm Hg or DBP ≥ 90 mm Hg) should be initiated on 2 first-line treatment agents with differing mechanisms of action
- They note that simultaneous use of an ACE inhibitor, ARB, and/or renin inhibitor is not recommended for hypertension in adults

# Angiotensin Modulators

- For resistant hypertension, AHA provides additional guidance with an initial focus on optimizing first-line therapies
- The ADA recommends initiation of pharmacologic therapy for patients with an office BP ≥ 130/80 mm Hg
- Patients with an office BP ≥ 150/90 mm Hg should be initiated on 2 medications (or a single-pill combination of drugs) which have been shown to reduce CV events in people with diabetes mellitus (DM)
- Treatment should include an ACE inhibitor or ARB, a CCB, and/or a thiazide-like diuretic

# Angiotensin Modulators

- Patients with coronary artery disease (CAD) or albuminuria should be prescribed an ACE inhibitor or an ARB as first-line therapy
- Per the American Academy of Pediatrics (APP), first line therapy options include an ACE inhibitor, ARB, long acting CCB, or thiazide diuretic for high blood pressure in children and adolescents
- According to the ACC, AHA, and Heart Failure Society of America (HFSA), patients with pre-HF (stage B) and with left ventricular ejection fraction (LVEF) ≤ 40% should be placed on an ACE inhibitor to prevent symptoms and to reduce mortality

# Angiotensin Modulators

- If a patient is intolerant to an ACE inhibitor and has a history of recent myocardial infarction (MI), an ARB should be used instead
- Patients with heart failure with reduced ejection fraction (HF*r*EF) and New York Heart Association (NYHA) class II to III symptoms are recommended to be placed on sacubitril/valsartan (Entresto) to reduce morbidity and mortality
- If treatment with an ARNI is not feasible, then an ACE inhibitor may be prescribed, or an ARB can be used if a patient is intolerant to an ACE inhibitor

# Angiotensin Modulators

- Treatment options that are potentially beneficial for patients with HF with preserved ejection fraction (HF*p*EF) with LVEF ≥ 50% include SGLT2 inhibitors, mineralocorticoid receptor antagonists (MRAs), ARBs, and ARNI
- Per the ACC, an ARB may be used for patients who cannot take an ARNI due to cost or intolerance
- Guidelines by the American Diabetes Association (ADA), the American Association of Clinical Endocrinologists (AACE), and ACC suggest that all patients with DM should receive an ACE inhibitor or ARB for the treatment of hypertension to reduce the risk of stroke and to delay the progression of diabetic nephropathy

# Angiotensin Modulators

- In patients with type 1 diabetes, hypertension, and nephropathy, long-term treatment with ACE inhibitors has been shown to reduce albuminuria and protect kidney function
- In patients with type 2 DM who have microalbuminuria, ACE inhibitors have been shown to reduce the urinary albumin excretion rate and mean arterial blood pressure
- ACE inhibitors and ARBs have been shown to delay the progression of nephropathy in patients with type 1 and type 2 diabetes

# Angiotensin Modulators

- ACE inhibitors have clearly been shown to prevent early death in diabetic patients
- Telmisartan (Micardis) and ramipril (Altace) were similar in reducing CV mortality in patients with vascular disease or high-risk DM
- The Kidney Disease Improving Global Outcomes (KDIGO) recommend the use of ARBs or other renin-angiotensin-system inhibitors for patients with CKD, diabetes, hypertension, and moderately to severely increased albuminuria

# Angiotensin Modulators

- In the setting of acute MI, ACE inhibitors have been shown to reduce mortality rates even in those with normal left ventricular function
- ACE inhibitors should be started and continued indefinitely in all patients recovering from ST-elevation myocardial infarction (STEMI) or unstable angina (UA)/non-ST-elevation myocardial infarction (NSTEMI) with LVEF of ≤ 40% and for those with hypertension, DM, or CKD
- ACE inhibitors are also considered a reasonable option in patients who are at lower risk
- ARBs are recommended in place of ACE inhibitors in those who are intolerant to ACE inhibitors

# Angiotensin Modulators

- According to the Agency for Healthcare Research and Quality (AHRQ), ACE inhibitors and ARBs appear to have similar long-term effects on blood pressure among individuals with essential hypertension
- It is possible that aliskiren may be more effective than ACE inhibitors (ramipril), but no differences were found in studies when compared to an ARB (losartan)
- There is insufficient evidence to determine if there are any different effects of ACE inhibitors versus ARBs on mortality and major CV events

# Angiotensin Modulators

- ACE inhibitors have been shown to have a greater risk of cough than ARBs and the direct renin inhibitor
- No significant difference in antihypertensive efficacy or adverse effect profiles among ACE inhibitor agents
- A network meta-analysis of ACE inhibitors for heart failure (HF) showed ramipril was associated with the lowest all-cause mortality
- In a study of HF patients, ramipril demonstrated lower mortality compared to enalapril and lisinopril

# Angiotensin Modulators

- Another study suggested that enalapril might be the most effective ACE inhibitor for improving certain heart function metrics, such as LVEF and stroke volume
- Enalapril was also associated with a higher rate of cough and renal function decline
- Some research suggests trandolapril is more successful at lowering both systolic and diastolic blood pressure than other ACE inhibitors
- Limited data suggest that candesartan (Atacand), valsartan (Diovan), and irbesartan (Avapro) at higher dosages offer greater decreases in blood pressure than losartan (Cozaar)

# Angiotensin Modulators

***Product/Guideline Updates***

- FDA announced that Boehringer Ingelheim made a business decision to discontinue Micardis (20 mg, 40 mg and 80 mg). Generics remain available
- FDA approved Vostally, an oral solution formulation of ramipril, indicated for:
  - Treatment of hypertension in adults, to lower blood pressure; lowering blood pressure reduces the risk of fatal and nonfatal CV events, primarily strokes and MI
  - In patients ≥ 55 years of age at high risk of developing a major CV event to reduce the risk of MI, stroke or death from CV causes
  - In adults with post-MI HF to reduce the risk of CV death & hospitalization for HF

# Angiotensin Modulator Combinations

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# Angiotensin Modulator Combinations

## FDA-Approved Indications

| Drug | Manufacturer | Indication(s) |
|---|---|---|
| amlodipine/benazepril (Lotrel®)[1] | generic, Novartis | Hypertension (not as initial therapy) |
| amlodipine/olmesartan (Azor®)[2] | generic, Cosette | ▪ Treatment of hypertension either alone or in combination with other agents<br>▪ Initial therapy in patients likely to need multiple antihypertensive agents to achieve their blood pressure (BP) goals |
| amlodipine/olmesartan/HCTZ (Tribenzor®)[3] | generic, Cosette | Hypertension (not as initial therapy) |
| amlodipine/perindopril (Prestalia®)[4] | Adhera | ▪ Treatment of hypertension for patients not adequately controlled on monotherapy<br>▪ Initial treatment of hypertension in patients who will likely require multiple medications for BP control |
| amlodipine/telmisartan[5] | generic | ▪ Treatment of hypertension alone or in combination with other agents<br>▪ Initial treatment of hypertension in patients who will likely require multiple medications for BP control |
| amlodipine/valsartan (Exforge®)[6] | generic, Novartis | ▪ Initial treatment of hypertension in patients who will likely require multiple medications for BP control<br>▪ Treatment of hypertension for patients not adequately controlled on monotherapy |
| amlodipine/valsartan/HCTZ (Exforge HCT®)[7] | generic, Novartis | Hypertension (not as initial therapy) |
| verapamil sustained-release (SR)/trandolapril[8] | Glenmark | Hypertension (not as initial therapy) |

HCTZ = hydrochlorothiazide

# Angiotensin Modulator Combinations

- The combination of an angiotensin modulator with a CCB has been shown to be more effective than either agent alone for the treatment of hypertension
- The combination products appear similar in efficacy and safety
- Per the AHA and ACC, first-line pharmacologic treatments for compelling indications (e.g., recent MI, angina) include ACE inhibitors, ARBs, or beta-blockers
- Additional medication classes including dihydropyridine CCBs, thiazide diuretics, and/or MRAs can be added as needed to achieve goal BP

# Angiotensin Modulator Combinations

## *Product/Guideline Updates*

- The FDA has approved Widaplik, a triple therapy combination containing telmisartan, amlodipine, and indapamide
- It is indicated for the treatment of hypertension, including as initial treatment, to lower blood pressure (lowering blood pressure reduces the risk of fatal and nonfatal CV events, primarily strokes and MIs)
- Carries a boxed warning for fetal toxicity
- Novartis will discontinue all strengths of Lotrel (amlodipine/benazepril) capsules. Generics remain available

# Anticonvulsants

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# 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

- Phenobarbital is indicated for insomnia, status epilepticus, and as a sedative
- Phenytoin (Dilantin, Phenytek) is indicated for prevention and treatment of seizures occurring during or following neurosurgery
- Clonazepam (Klonopin) is indicated for panic disorder
- 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 that are distinct from the patient's typical seizure pattern
- Carbamazepine (Equetro) is approved for mixed-type seizures

# Anticonvulsants

## Other Epilepsy Indications

- Cannabidiol solution (Epidiolex) is approved for the treatment of seizures associated with Dravet syndrome and seizures associated with tuberous sclerosis complex
- Fenfluramine (Fintepla) and stiripentol (Diacomit) are approved for the treatment of seizures associated with Dravet syndrome
- Ganaxolone (Ztalmy) is approved for the treatment of seizures associated with cyclin-dependent kinase-like 5 (CDKL5) deficiency disorder (CDD)
- Pregabalin (Lyrica) is indicated for treatment of fibromyalgia
- Vigabatrin (Sabril) is indicated for the treatment of infantile spasms when the potential benefit outweighs the risk of potential vision loss

# Anticonvulsants

- Epilepsy affects 3.4 million Americans
- The American Epilepsy Society (AES) and the American Academy of Neurology (AAN) 2018 (reaffirmed in 2024) guidelines suggest 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
- Ethosuximide or a valproic acid derivative should be considered before lamotrigine in newly diagnosed childhood absence epilepsy

# Anticonvulsants

- Immediate release pregabalin (Lyrica) and perampanel (Fycompa) are recommended as first-line treatment, while vigabatrin (Sabril) and rufinamide (Banzel) as second-line therapies for treatment-resistant focal epilepsy
- Lacosamide (Vimpat), eslicarbazepine (Aptiom), and ER topiramate should also be considered for this population
- For patients with Lennox-Gastaut syndrome, AAN recommends lamotrigine and topiramate
- Add-on therapy for Lennox-Gastaut includes cannabidiol (Epidiolex), clobazam (Onfi, Sympazan), felbamate (Felbatol), lamotrigine (Lamictal, Lamictal XR), rufinamide (Banzel), and topiramate (Eprontia, Qudexy XR, Topamax, Trokendi XR)
- IR and ER lamotrigine should be considered for adult with treatment-resistant generalized tonic-clonic seizures

# Anticonvulsants

- Levetiracetam (Keppra) has a role as adjunctive therapy in treatment-resistant childhood focal epilepsy, generalized tonic-clonic seizures, and juvenile myoclonic epilepsy
- Zonisamide (Zonegran, Zonisade) should be considered for patients aged 6 to 17 years and oxcarbazepine for patients aged one month to four years with treatment-resistant childhood focal epilepsy
- 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
- In adults with convulsive status epilepticus, IM midazolam and IV lorazepam, diazepam, and phenobarbital are efficacious
- In children, IV lorazepam and diazepam *are* effective at stopping these seizures, while rectal diazepam and midazolam (IM, intranasal, and buccal) are *probably* effective

# Anticonvulsants

- Cannabidiol (Epidiolex), stiripentol (Diacomit), and fenfluramine (Fintepla) are indicated for Dravet syndrome
- As for seizures associated with CDKL5 CDD, ganaxolone (Ztalmy) is approved for this condition
- Other medications frequently used are levetiracetam, topiramate, clobazam, and phenobarbital
- About 70% of patients with epilepsy can be maintained on 1 drug
- If control is not achieved with 1 drug, an alternative medication should be attempted before others are added to current therapy
- Anticonvulsants have very little or no direct comparative data in the treatment of seizures or any other indication

# Anticonvulsants

## *Product/Guideline Updates*

- Upsher-Smith will be discontinuing brand name Qudexy XR (topiramate capsule ER); generic product will continue to be provided from this manufacturer
- Valtoco (diazepam) is now approved for the acute treatment of intermittent, stereotypic episodes of frequent seizure activity that are distinct from a patient's usual seizure pattern to include patients with epilepsy who are ≥ 2 years of age
- FDA has approved the first generic to Catalyst's Fycompa from Teva

# Antifungals, Oral

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# 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

- 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 U.S.

# Antifungals, Oral

- It is estimated that treatment with azole antifungals provides relief of symptoms and negative cultures in 80% to 90% of patients with uncomplicated VVC
- 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

# Antifungals, Oral

- Posaconazole oral suspension has an indication for treatment of oropharyngeal candidiasis when refractory to itraconazole and/or fluconazole
- 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, Topical

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# 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
- Limited data are available regarding comparative efficacy in the treatment of the various fungal infections, including tinea cruris, tinea corporis, tinea pedis, and tinea versicolor

# Antifungals, Topical

- Combination therapy (antifungal plus corticosteroid) can be considered when inflammation is present
- 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

# Antihistamines, Minimally Sedating

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# Antihistamines, Minimally Sedating

## FDA-Approved Indications

| Drug | Rx/OTC | Manufacturer | Indication(s) |
|---|---|---|---|
| cetirizine capsules, tablets, oral liquid | Rx<br>generic cetirizine oral liquid<br>OTC<br>generic chewable tablet, liquid gel, oral liquid, tablet<br>Zyrtec® (all formulations) | generic,<br>J&J Consumer | ▪ Temporary relief of symptoms due to hay fever or other respiratory allergies (sneezing; runny nose; itchy, watery eyes; itchy throat or nose) in adults and children ages ≥ 2 years<br>▪ Relief of symptoms associated with seasonal AR due to allergens such as ragweed, grass, and tree pollens in adults and children ages ≥ 2 years<br>▪ Relief of symptoms associated with perennial AR due to allergens such as dust mites, animal dander, and molds in adults and children ages ≥ 6 months<br>▪ Treatment of uncomplicated skin manifestations of chronic idiopathic urticaria (CIU) in adults and children ages ≥ 6 months |
| cetirizine ODT<br>(Zyrtec® Allergy ODT) | OTC | generic,<br>J&J Consumer | ▪ Temporary relief of symptoms of upper respiratory allergies (sneezing; runny nose; itchy, watery eyes; itchy throat or nose) in adults and children ages ≥ 6 months<br>▪ Relief of itching due to urticaria in patients in adults and children ages ≥ 6 months |
| cetirizine/pseudoephedrine<br>(Zyrtec-D® OTC 12 Hour) | OTC | generic,<br>J&J Consumer | ▪ Temporary relief of symptoms associated with sinusitis, allergic rhinitis, and other upper respiratory allergies (nasal congestion, sneezing; runny nose; itchy, watery eyes; itchy throat or nose) in adults and children ages ≥ 12 years |

# Antihistamines, Minimally Sedating

| | | | |
|---|---|---|---|
| desloratadine tablet (Clarinex®, Clarinex Redi-Tabs®) | Rx | generic, Organon | ▪ Relief of nasal and non-nasal symptoms of seasonal AR in patients ages ≥ 2 years<br>▪ Relief of nasal and non-nasal symptoms of perennial AR in patients ages ≥ 6 months<br>▪ Symptomatic relief of pruritus, reduction in the number of hives, and size of hives in patients with CIU ages ≥ 6 months |
| desloratadine ODT | Rx | generic | ▪ Relief of nasal and non-nasal symptoms of seasonal AR in patients ages ≥ 2 years<br>▪ Relief of nasal and non-nasal symptoms of perennial AR in patients ages ≥ 6 months |
| desloratadine/ pseudoephedrine (Clarinex-D® 12-Hour) | Rx | Organon | ▪ Relief of nasal and non-nasal symptoms of seasonal AR, including nasal congestion in adults and children ages ≥ 12 years |
| fexofenadine (Allegra®) | OTC | generic, Chattem Consumer | ▪ Relief of symptoms associated with hay fever or other upper respiratory allergies (sneezing; runny nose; itchy, watery eyes; itchy throat or nose) in adults and children ages ≥ 12 years |
| fexofenadine oral suspension | OTC | Generic | |

# Antihistamines, Minimally Sedating

| Drug | Rx/OTC | Manufacturer | Indication(s) |
|---|---|---|---|
| fexofenadine ODT<br>(Allegra ODT®) | OTC | Chattem Consumer | ▪ Relief of symptoms associated with hay fever or other upper respiratory allergies (sneezing; runny nose; itchy, watery eyes; itchy throat or nose) in adults and children ages ≥ 6 years |
| fexofenadine/pseudoephedrine<br>(Allegra-D® 12 and 24 Hour) | OTC | generic,<br>Chattem Consumer | ▪ Relief of symptoms associated with seasonal AR in adults and children ages ≥ 12 years |
| levocetirizine tablet, oral liquid | Rx | generic | ▪ Relief of symptoms associated with perennial AR in adults and children ages 6 months to 2 years<br>▪ Treatment of uncomplicated skin manifestations of CIU in adults and children ages ≥ 6 months |
| levocetirizine tablet<br>(Xyzal® Allergy 24HR) | OTC | generic, Chattem Consumer | ▪ Temporary relief of runny nose, sneezing, itchy/watery eyes, and itching of the nose or throat due to hay fever or other respiratory allergies in patients 6 to 64 years of age |
| levocetirizine syrup<br>(Children's Xyzal® Allergy 24HR; Xyzal Allergy 24HR) | OTC | Chattem Consumer | ▪ Temporary relief of runny nose, sneezing, itchy/watery eyes, and itching of the nose or throat due to hay fever or other respiratory allergies in patients ages ≥ 2 years |
| loratadine tablet, ODT, liquid, capsule<br>(Alavert®, Claritin®, Claritin Redi-Tabs, Claritin® Liqui-Gels) | OTC | generic,<br>Pfizer Consumer,<br>Bayer/Schering-Plough | ▪ Temporary relief of symptoms due to hay fever or other respiratory allergies in adults and children ages ≥ 6 years |
| loratadine chewable tablet, ODT, syrup<br>(Children's Claritin®; Claritin Chewable) | OTC | Bayer/Schering-Plough | ▪ Temporary relief of symptoms due to hay fever or other respiratory allergies in patients ages ≥ 2 years<br>▪ Treatment of CIU in patients ages ≥ 2 years |
| loratadine/pseudoephedrine<br>(Claritin-D® 12 Hour, Claritin-D® 24 Hour) | OTC | generic,<br>Foundation Consumer<br>Pfizer Consumer<br>Bayer/Schering-Plough | ▪ Temporary relief of symptoms (sinus nasal congestion, runny nose, sneezing, itchy nose, watery eyes) due to common cold, hay fever, or other respiratory allergies or sinusitis in adults and children ages ≥ 12 years |

Rx = prescription required; OTC = over-the-counter; ODT = orally disintegrating tablet

# Antihistamines, Minimally Sedating

- Allergic rhinitis (AR) affects 10% and 30% of adults and up to 40% of children in the U.S.
- AR is characterized by sneezing, itching of the eyes, nose, ears and palate, and rhinorrhea
- Symptoms develop when patients inhale airborne antigens to which they have previously been exposed and have made antibodies
- Seasonal AR generally occurs in the spring, summer, and early fall
- Perennial AR is an IgE-mediated reaction to allergens resulting in symptoms year-round and is usually caused by dust mites, pet hair, dander, mold, or cockroaches

# Antihistamines, Minimally Sedating

- Non-allergic rhinitis usually affects adults and results in year-round symptoms
- Its causes can include strong odors, polluted air, smoke, and other irritants
- Oral antihistamines are particularly effective for severe rhinorrhea, sneezing, pruritus, and conjunctivitis associated with AR, although less effective for nasal congestion
- For patients with more significant nasal congestion, several of the minimally sedating antihistamines are available as combination dosage forms with a decongestant

# Antihistamines, Minimally Sedating

- These minimally sedating (second-generation) antihistamines are generally considered before sedating (first-generation) antihistamines because they are associated with a lower incidence of side effects
- According to the American Academy of Allergy, Asthma, and Immunology (AAAAI), oral antihistamines are considered most effective for treatment for seasonal and perennial AR when used continuously
- Antihistamines, dosed when needed, can be an appropriate treatment option for episodic AR
- Oral antihistamines are as effective as intranasal corticosteroids for the treatment of ocular symptoms, but are less effective than intranasal corticosteroids for nasal congestion and AR symptoms

# Antihistamines, Minimally Sedating

- Per the American Academy of Otolaryngology – Head and Neck Surgery, oral minimally sedating antihistamines are strongly recommended for patients with primary complaints of sneezing and itching
- Minimally sedating antihistamines are generally considered first-line therapy for Chronic Idiopathic Urticaria (CIU)
- Some studies indicate cetirizine may be more effective than loratadine at providing symptomatic relief
- Current data suggest the least likelihood of sedation is with fexofenadine or desloratadine

# Antimigraine Agents, Triptans

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# 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 U.S.
- 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, 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 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
- Triptans appear to be equally safe

# Antimigraine Agents, Triptans

- American College of Physicians (ACP) has published a guideline in 2025 on pharmacologic treatments for acute episodic migraine headache in the outpatient setting
- A triptan is *recommended* to be added to an NSAID to treat moderate to severe acute episodic migraine headache for non-pregnant adults who do not have a sufficient response to an NSAID (*strong recommendation; moderate-certainty evidence*)
- It is *suggested* to add a triptan to acetaminophen for the treatment of moderate to severe acute episodic migraine headache for nonpregnant adults who do not have a sufficient response to acetaminophen (*conditional recommendation; low-certainty evidence)*

# Antimigraine Agents, Triptans

- For prevention of episodic migraine in non-pregnant adults in outpatient settings, this guideline suggests monotherapy with a beta blocker (e.g., metoprolol, propranolol), valproate, venlafaxine, or amitriptyline
- Patients who do not tolerate or have an inadequate response to these medications are suggested to be given monotherapy with a calcitonin gene-related peptide (CGRP) antagonist-gepant or CGRP monoclonal antibody
- Patients who do not respond to any of these therapies are suggested to be prescribed topiramate

# Antimigraine Agents, Triptans

- Frovatriptan is established for short-term menstrually-associated migraine (MAM) prevention
- 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

# Beta Blockers

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

- Beta blockers have similar efficacy for the treatment of HTN
- Beta blockers are one of the classes suggested as first-line therapy in patients with CAD, post-MI, and HF
- 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

- Per the APP, beta blockers are not recommended as initial pharmacologic treatment in children
- Beta blockers prevent recurrent ischemia, life-threatening ventricular arrhythmias, reduce the incidence of sudden cardiac death, and improve survival in patients with prior MI
- The 2023 ACC/AHA guidelines for chronic stable angina, now termed chronic coronary disease (CCD), recommend either a beta blocker or CCB for antianginal therapy
- Beta blockers have a Class 1 recommendation for patients with CCD and a LVEF≤40% with or without previous MI

# Beta Blockers

- They also highlight that beta blockers are no longer recommended for indefinite use following a MI unless other conditions like low LVEF are present
- Per the 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure, in patients with HF*r*EF, with current or previous symptoms, the use of 1 of the 3 beta blockers proven to reduce mortality (e.g., bisoprolol, carvedilol, sustained-release metoprolol succinate) is recommended to reduce mortality and hospitalizations

# BPH Treatments

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# 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)

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

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

# BPH Treatments

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

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

***Class Overview: Phosphodiesterase 5 (PDE5) Inhibitors***

- tadalafil - (Cialis, tadalafil)

***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 U.S. 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 intra-operative floppy iris syndrome and should discuss these risks with their ophthalmologist
- The guidelines also state that the 5-alpha reductase inhibitors (5ARs), finasteride (Proscar) and dutasteride (Avodart) should be used alone or in combination with an alpha blocker for patients with LUTS 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 intra-operative bleeding and peri- or post-operative need for blood transfusion after transurethral resection of the prostate (TURP) or other surgical intervention for BPH
- For patients with LUTS/BPH, regardless of comorbid erectile dysfunction (ED), 5 mg daily tadalafil is also a potential treatment option
- 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
- 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/Guideline Updates***

- Abbvie is discontinuing Rapaflo capsules (4 mg, 8 mg. Generics remain available
- FDA issued alert regarding potential risks associated with compounded topical finasteride products
- FDA approved a generic to Blue Water Biotech's Entadfi

# Calcium Channel Blockers

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# 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 hypertension in the non-African American population is a thiazide-type diuretic, a CCB, an ACE inhibitor, or an 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

# Calcium Channel Blockers

- Diltiazem decreases atrioventricular (AV) conduction and heart rate
- Verapamil decreases heart rate, slows AV 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
- In patients with hypertension and a known risk factor for CAD, the ALLHAT 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 Update***

- FDA approved nimodipine 6 mg/mL, the first generic for Azurity's Nymalize 6 mg/mL oral solution

# Contraceptives

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# Contraceptives, Oral

## *Products Listing*

| LABEL NAME | MANUFACTURER | DRUG TYPE |
|---|---|---|
| AFIRMELLE-28 TABLET | AUROBINDO PHARM | GEN |
| ALTAVERA-28 TABLET | XIROMED, LLC | GEN |
| ALYACEN 1-35 28 TABLET | GLENMARK PHARMA | GEN |
| ALYACEN 7-7-7-28 TABLET | GLENMARK PHARMA | GEN |
| AMETHIA 0.15-0.03-0.01 MG TAB | MAYNE PHARMA IN | GEN |
| AMETHYST 90-20 MCG TABLET | TEVA PHARM | BWG |
| APRI 28 DAY TABLET | TEVA USA | GEN |
| ARANELLE 28 TABLET | TEVA USA | GEN |
| ASHLYNA 0.15-0.03-0.01 MG TAB | GLENMARK PHARMA | GEN |
| AUBRA EQ-28 TABLET | AFAXYS, INC. | GEN |
| AUBRA-28 TABLET | AFAXYS, INC. | GEN |
| AUROVELA 1 MG-20 MCG TABLET | AUROBINDO PHARM | GEN |
| AUROVELA 21 1.5-30 TABLET | AUROBINDO PHARM | GEN |
| AUROVELA 24 FE 1 MG-20 MCG TAB | AUROBINDO PHARM | GEN |
| AUROVELA FE 1-20 TABLET | AUROBINDO PHARM | GEN |
| AUROVELA FE 1.5 MG-30 MCG TAB | AUROBINDO PHARM | GEN |
| AVERI 0.15-0.03 MG 28 DAY TAB | AVION PHARMACEU | SSB |
| AVIANE-28 TABLET | TEVA USA | GEN |

# Contraceptives, Oral

## *Products Listing*

| | | |
|---|---|---|
| AYUNA-28 TABLET | AUROBINDO PHARM | GEN |
| AZURETTE 28 DAY TABLET | DR.REDDY'S LAB | GEN |
| BALCOLTRA TABLET | AVION PHARMACEU | SSB |
| BALZIVA 28 TABLET | TEVA USA | GEN |
| BEYAZ 28 TABLET | BAYER,PHARM DIV | SSB |
| BLISOVI 24 FE TABLET | LUPIN PHARMACEU | GEN |
| BLISOVI FE 1-20 TABLET | LUPIN PHARMACEU | GEN |
| BLISOVI FE 1.5-30 TABLET | LUPIN PHARMACEU | GEN |
| BRIELLYN TABLET | GLENMARK PHARMA | GEN |
| CAMILA 0.35 MG TABLET | generic | GEN |
| CAMRESE 0.15-0.03-0.01 MG TAB | TEVA USA | GEN |
| CAMRESE LO TABLET | TEVA USA | GEN |
| CAZIANT 28 DAY TABLET | MAYNE PHARMA IN | GEN |
| CHARLOTTE 24 FE CHEWABLE TAB | GLENMARK PHARMA | GEN |
| CHATEAL EQ-28 TABLET | AFAXYS, INC. | GEN |
| CRYSELLE-28 TABLET | TEVA USA | GEN |

# Contraceptives, Oral

## *Products Listing*

| | | |
|---|---|---|
| CYRED 28 DAY TABLET | AFAXYS, INC. | GEN |
| CYRED EQ 28 DAY TABLET | AFAXYS, INC. | BWG |
| DASETTA 1-35-28 TABLET | NORTHSTAR RX LL | GEN |
| DASETTA 7/7/7-28 TABLET | NORTHSTAR RX LL | GEN |
| DAYSEE 0.15-0.03-0.01 MG TAB | LUPIN PHARMACEU | GEN |
| DEBLITANE 0.35 MG TABLET | NORTHSTAR RX LL | GEN |
| DESOGESTR-ETH ESTRAD ETH ESTRA | MYL-VIA/XIROMED | GEN |
| DOLISHALE 90-20 MCG TABLET | INGENUS PHARMAC | GEN |
| DROSP-EE-LEVOMEF 3-0.02-0.451 | generic | GEN |
| DROSP-EE-LEVOMEF 3-0.03-0.451 | SANDOZ | GEN |
| DROSPIRENONE-EE 3-0.02 MG TAB | generic | GEN |
| DROSPIRENONE-EE 3-0.03 MG TAB | generic | GEN |
| DROSPIRENONE-EE 3-0.03 MG TAB | generic | GEN |
| ECONTRA EZ 1.5 MG TABLET | AFAXYS, INC. | GEN |
| ECONTRA ONE-STEP 1.5 MG TABLET | AFAXYS, INC. | GEN |
| ELINEST-28 TABLET | NORTHSTAR RX LL | GEN |

# Contraceptives, Oral

## *Products Listing*

| | | |
|---|---|---|
| ELLA 30 MG TABLET | HRA PHARMA AMER | BWG |
| EMZAHH 0.35 MG TABLET | AUROBINDO PHARM | GEN |
| ENPRESSE-28 TABLET | TEVA USA | SSB |
| ENSKYCE 28 TABLET | LUPIN PHARMACEU | GEN |
| ERRIN 0.35 MG TABLET | generic | GEN |
| ESTARYLLA 0.25-0.035 MG TABLET | XIROMED, LLC | GEN |
| DROSPIRENONE-EE 3-0.02 MG TAB | generic | GEN |
| DROSPIRENONE-EE 3-0.03 MG TAB | generic | GEN |
| DROSPIRENONE-EE 3-0.03 MG TAB | generic | GEN |
| ETHYNODIOL-ETH ESTRA 1MG-35MCG | MYL-VIA/XIROMED | GEN |
| ETHYNODIOL-ETH ESTRA 1MG-50MCG | MYL-VIA/XIROMED | GEN |
| FALMINA-28 TABLET | NORTHSTAR RX LL | GEN |
| FEIRZA 1 MG-20 MCG TABLET | XIROMED, LLC | GEN |
| FEIRZA 1.5 MG-30 MCG TABLET | XIROMED, LLC | GEN |
| FEMLYV 1 MG-0.02 MG ODT | MILLICENT PHARM | SSB |
| FINZALA 1-0.02(24)-75 CHEW TAB | TEVA USA | BWG |
| GALBRIELA 0.8-0.025 MG CHEW TB | XIROMED, LLC | GEN |
| GEMMILY 1 MG-20 MCG CAPSULE | XIROMED, LLC | GEN |
| HAILEY 24 FE 1 MG-20 MCG TAB | GLENMARK PHARMA | GEN |
| HAILEY FE 1.5-30 TABLET | GLENMARK PHARMA | GEN |
| HAILEY FE 1-20 TABLET | GLENMARK PHARMA | GEN |

# Contraceptives, Oral

## *Products Listing*

| | | | |
|---|---|---|---|
| HAILEY 21 1.5 MG-30 MCG TAB | GLENMARK PHARMA | GEN | |
| HEATHER 0.35 MG TABLET | GLENMARK PHARMA | GEN | |
| ICLEVIA 0.15 MG-0.03 MG TABLET | AUROBINDO PHARM | GEN | |
| INCASSIA 0.35 MG TABLET | AUROBINDO PHARM | GEN | |
| INTROVALE 0.15-0.03 MG TABLET | XIROMED, LLC | GEN | |
| ISIBLOOM 28 DAY TABLET | XIROMED, LLC | GEN | |
| JAIMIESS 0.15-0.03-0.01 MG TAB | XIROMED, LLC | GEN | |
| JASMIEL 3 MG-0.02 MG TABLET | AFAXYS, INC. | GEN | |
| JENCYCLA 0.35 MG TABLET | LUPIN PHARMACEU | GEN | |
| JOLESSA 0.15 MG-0.03 MG TABLET | TEVA USA | BWG | |
| JOYEAUX-28 TABLET | XIROMED, LLC | GEN | |
| JULEBER 28 DAY TABLET | NORTHSTAR RX LL | GEN | |
| JUNEL 1 MG-20 MCG TABLET | TEVA USA | GEN | |
| JUNEL 1.5 MG-30 MCG TABLET | TEVA USA | GEN | |
| JUNEL FE 1 MG-20 MCG TABLET | TEVA USA | GEN | |
| JUNEL FE 1.5 MG-30 MCG TABLET | TEVA USA | GEN | |
| JUNEL FE 24 TABLET | TEVA USA | GEN | |

# Contraceptives, Oral

## *Products Listing*

| | | |
|---|---|---|
| KAITLIB FE 0.8-0.025MG CHEW TB | LUPIN PHARMACEU | GEN |
| KALLIGA 28 DAY TABLET | AUROBINDO PHARM | GEN |
| KARIVA 28 DAY TABLET | TEVA USA | GEN |
| KELNOR 1-35 28 TABLET | TEVA USA | SSB |
| KELNOR 1-35 28 TABLET | TEVA USA | GEN |
| KURVELO-28 TABLET | LUPIN PHARMACEU | GEN |
| LARIN 1.5 MG-30 MCG TABLET | NORTHSTAR RX LL | GEN |
| LARIN 21 1-20 TABLET | NORTHSTAR RX LL | GEN |
| LARIN 24 FE 1 MG-20 MCG TABLET | NORTHSTAR RX LL | GEN |
| LARIN FE 1.5-30 TABLET | NORTHSTAR RX LL | GEN |
| LARIN FE 1-20 TABLET | NORTHSTAR RX LL | GEN |
| LEENA 28 TABLET | MAYNE PHARMA IN | SSB |
| LESSINA-28 TABLET | TEVA USA | GEN |
| LEVONEST-28 TABLET | NORTHSTAR RX LL | GEN |
| LEVONORG-EE-FE BIS 0.1-0.02-36 | ACELLA PHARMACE | GEN |
| LEVONORGESTREL 1.5 MG TABLET | generic | GEN |
| LEVONOR-ETH ESTRA 0.09-0.02 MG | GLENMARK PHARMA | GEN |

# Contraceptives, Oral

## *Products Listing*

| | | |
|---|---|---|
| LEVONOR-ETH ESTRAD 0.15-0.03 | generic | GEN |
| LEVONOR-E ESTRAD 0.1-0.02-0.01 | generic | GEN |
| LEVONOR-ETH ESTRAD 0.1-0.02 MG | generic | GEN |
| LEVONOR-ETH ESTRAD 0.1-0.02 MG | generic | GEN |
| LEVONOR-ETH ESTRAD 0.15-0.03 | generic | GEN |
| LEVONOR-ETH ESTRAD TRIPHASIC | LUPIN PHARMACEU | GEN |
| LEVORA-28 TABLET | MAYNE PHARMA IN | GEN |
| LO LOESTRIN FE 1-10 TABLET | ACTAVIS/ALLERGA | SSB |
| LOESTRIN 21 1.5-30 TABLET | TEVA WOMEN'S HE | BWG |
| LOESTRIN 21 1-20 TABLET | TEVA WOMEN'S HE | BWG |
| LOESTRIN FE 1.5-30 TABLET | TEVA WOMEN'S HE | BWG |
| LOESTRIN FE 1-20 TABLET | TEVA WOMEN'S HE | BWG |
| LOJAIMIESS 0.1-0.02-0.01 TAB | XIROMED, LLC | GEN |
| LORYNA 3 MG-0.02 MG TABLET | XIROMED, LLC | GEN |
| LOW-OGESTREL-28 TABLET | MAYNE PHARMA IN | GEN |
| LO-ZUMANDIMINE 3 MG-0.02 MG TB | AUROBINDO PHARM | GEN |
| LUIZZA 1 MG-20 MCG TABLET | XIROMED, LLC | GEN |
| LUIZZA 1.5 MG-30 MCG TABLET | XIROMED, LLC | GEN |

# Contraceptives, Oral

## *Products Listing*

| | | |
|---|---|---|
| LUTERA-28 TABLET | MAYNE PHARMA IN | GEN |
| LYLEQ 0.35 MG TABLET | AFAXYS, INC. | GEN |
| LYZA 0.35 MG TABLET | AFAXYS, INC. | GEN |
| MARLISSA-28 TABLET | GLENMARK PHARMA | GEN |
| MELEYA 0.35 MG TABLET | XIROMED, LLC | GEN |
| MERZEE 1 MG-20 MCG CAPSULE | LUPIN PHARMACEU | GEN |
| MIBELAS 24 FE CHEWABLE TABLET | LUPIN PHARMACEU | GEN |
| MICROGESTIN 21 1.5-30 TAB | DR.REDDY'S LAB | GEN |
| MICROGESTIN 21 1-20 TABLET | generic | GEN |
| MICROGESTIN FE 1.5-30 TAB | DR.REDDY'S LAB | GEN |
| MICROGESTIN FE 1-20 TABLET | DR.REDDY'S LAB | GEN |
| MILI 0.25-0.035 MG TABLET | AUROBINDO PHARM | GEN |
| MINZOYA-28 TABLET | LUPIN PHARMACEU | GEN |
| MONO-LINYAH 28 TABLET | NORTHSTAR RX LL | BWG |
| MY CHOICE 1.5 MG TABLET | SUN PHARMACEUTI | GEN |
| MY WAY 1.5 MG TABLET | LUPIN PHARMACEU | GEN |

# Contraceptives, Oral

## *Products Listing*

| | | |
|---|---|---|
| NATAZIA 28 TABLET | BAYER,PHARM DIV | SSB |
| NECON 0.5-35-28 TABLET | DR.REDDY'S LAB | GEN |
| NEW DAY 1.5 MG TABLET | NORTHSTAR RX LL | GEN |
| NEXTSTELLIS 3-14.2 MG TABLET | MAYNE PHARMA IN | SSB |
| NIKKI 3 MG-0.02 MG TABLET | LUPIN PHARMACEU | GEN |
| NORA-BE TABLET | TEVA USA | BWG |
| NORETHINDRONE 0.35 MG TABLET | generic | GEN |
| NORETHIND-ETH ESTRAD 1-0.02 MG | generic | GEN |
| NORETHIN-EE 1.5-0.03 MG(21) TB | MYL-VIA/XIROMED | GEN |
| NORETH-EE-FE 1.5-0.03MG(21)-75 | MYL-VIA/XIROMED | GEN |
| NORETH-EE-FE 1-0.02(24)-75 CAP | GLENMARK PHARMA | GEN |
| NORETH-EE-FE 1-0.02(24)-75 CHW | XIROMED, LLC | GEN |
| NORETHIN-ESTRA-FE 0.8-0.025 MG | MYL-VIA/XIROMED | GEN |
| NORG-ETHIN ESTRA 0.25-0.035 MG | generic | GEN |
| NORG-EE 0.18-0.215-0.25/0.035 | generic | GEN |
| NORTREL 0.5-35-28 TABLET | TEVA USA | GEN |
| NORTREL 1-35 21 TABLET | TEVA USA | GEN |
| NORTREL 1-35 28 TABLET | TEVA USA | GEN |
| NORTREL 7-7-7-28 TABLET | TEVA USA | GEN |

# Contraceptives, Oral

## *Products Listing*

| | | |
|---|---|---|
| NYLIA 1-35 28 TABLET | AUROBINDO PHARM | GEN |
| NYLIA 7-7-7-28 TABLET | AUROBINDO PHARM | GEN |
| OPCICON ONE-STEP 1.5 MG TABLET | SUN PHARMACEUTI | GEN |
| OPILL 0.075 MG TABLET | PERRIGO CO. | SSB |
| OPTION 2 1.5 MG TABLET | PERRIGO CO. | GEN |
| ORQUIDEA 0.35 MG TABLET | XIROMED, LLC | GEN |
| ORTHO TRI-CYCLEN 28 TABLET | JANSSEN PHARM. | BWG |
| ORTHO-NOVUM 7-7-7-28 TABLET | JANSSEN PHARM. | SSB |
| PHILITH 0.4-0.035 MG TABLET | NORTHSTAR RX LL | GEN |
| PIMTREA 28 DAY TABLET | NORTHSTAR RX LL | GEN |
| PORTIA-28 TABLET | TEVA USA | GEN |
| RECLIPSEN 28 DAY TABLET | TEVA USA | GEN |
| RIVELSA TABLET | TEVA USA | GEN |
| ROSYRAH TABLET | XIROMED, LLC | GEN |
| SAFYRAL TABLET | BAYER,PHARM DIV | SSB |

# Contraceptives, Oral

## *Products Listing*

| | | | |
|---|---|---|---|
| SETLAKIN 0.15 MG-0.03 MG TAB | NORTHSTAR RX LL | GEN | S |
| SHAROBEL 0.35 MG TABLET | NORTHSTAR RX LL | GEN | S |
| SIMLIYA 28 DAY TABLET | AUROBINDO PHARM | GEN | S |
| SIMPESSE 0.15-0.03-0.01 MG TAB | AUROBINDO PHARM | GEN | S |
| SLYND 4 MG TABLET | EXELTIS USA, IN | SSB | S |
| SPRINTEC 28 DAY TABLET | TEVA USA | GEN | S |
| SRONYX 0.10-0.02 MG TABLET | MAYNE PHARMA IN | GEN | S |
| SYEDA 28 TABLET | XIROMED, LLC | GEN | S |
| TARINA 24 FE 1 MG-20 MCG TAB | AFAXYS, INC. | GEN | T |
| TARINA FE 1-20 TABLET | AFAXYS, INC. | GEN | T |
| TARINA FE 1-20 EQ TABLET | AFAXYS, INC. | GEN | T |
| TAYTULLA 1 MG-20 MCG CAPSULE | ALLERGAN INC. | SSB | T |
| TILIA FE 28 TABLET | DR.REDDY'S LAB | GEN | T |
| TRI-ESTARYLLA TABLET | XIROMED, LLC | SSB | T |
| TRI-LEGEST FE-28 DAY TABLET | TEVA USA | GEN | T |
| TRI-LINYAH TABLET | NORTHSTAR RX LL | BWG | T |
| TRI-LO-ESTARYLLA TABLET | XIROMED, LLC | GEN | T |

# Contraceptives, Oral

## *Products Listing*

| | | |
|---|---|---|
| TRI-LO-MARZIA TABLET | LUPIN PHARMACEU | GEN |
| TRI-LO-MILI TABLET | AUROBINDO PHARM | GEN |
| TRI-LO-SPRINTEC TABLET | TEVA USA | GEN |
| TRI-MILI 28 TABLET | AUROBINDO PHARM | GEN |
| TRI-SPRINTEC TABLET | TEVA USA | GEN |
| TRI-VYLIBRA 28 TABLET | AFAXYS, INC. | GEN |
| TRI-VYLIBRA LO TABLET | AFAXYS, INC. | GEN |
| TULANA 0.35 MG TABLET | AFAXYS, INC. | GEN |
| TURQOZ-28 TABLET | LUPIN PHARMACEU | GEN |
| TYBLUME 0.1-0.02 MG CHEW TAB | EXELTIS USA, IN | BWG |
| VALTYA 1 MG-35 MCG TABLET | XIROMED, LLC | GEN |
| VALTYA 1 MG-50 MCG TABLET | XIROMED, LLC | GEN |
| VELIVET 28 DAY TABLET | TEVA USA | GEN |
| VESTURA 3 MG-0.02 MG TABLET | generic | GEN |
| VIENVA-28 TABLET | XIROMED, LLC | GEN |
| VIORELE 28 DAY TABLET | GLENMARK PHARMA | GEN |
| VOLNEA 0.15-0.02-0.01 MG TAB | XIROMED, LLC | GEN |

# Contraceptives, Oral

***Products Listing***

| | | |
|---|---|---|
| VYFEMLA 0.4 MG-0.035 MG TABLET | LUPIN PHARMACEU | BWG |
| VYLIBRA 28 TABLET | AFAXYS, INC. | GEN |
| WERA 0.5/0.035 MG 28 TABLET | NORTHSTAR RX LL | GEN |
| WYMZYA FE 0.4-0.035 MG CHEW TB | LUPIN PHARMACEU | BWG |
| XARAH FE 1 MG/20-30-35 MCG TAB | XIROMED, LLC | GEN |
| XELRIA FE 0.4-0.035 MG CHEW TB | XIROMED, LLC | GEN |
| YASMIN 28 TABLET | BAYER,PHARM DIV | BWG |
| YAZ 28 TABLET | BAYER,PHARM DIV | BWG |
| ZARAH TABLET | MAYNE PHARMA IN | GEN |
| ZOVIA 1-35 TABLET | DR.REDDY'S LAB | GEN |
| ZUMANDIMINE 3 MG-0.03 MG TAB | AUROBINDO PHARM | GEN |

# Contraceptives, Other

- ***Class Overview: Vaginal***
  - etonogestrel/ethinyl estradiol ring - (Nuvaring, Eluryng, Enilloring, Aloette)
  - egesterone acetate/ethinyl estradiol ring - (Annovera)
  - lactic acid/citric acid/potassium bitartrate gel - (Phexxi)

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

- ***Class Overview: Copper IUD***
  - copper IUD - (Paragard; Miudella)

# Contraceptives, Other

- ***Class Overview:  Implants***
  - etonogestrel implant - (Nexplanon)

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

- ***Class Overview: Transdermal***
  - norelgestromin/ethinyl estradiol weekly patch– (Xulane***;*** Zafemy)
  - levonorgestrel/ethinyl estradiol weekly patch – (Twirla)

# Contraceptives, Other

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

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

# 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)
- 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

# 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 thromboembolism (VTE) risk
- Some OCs have additional indications or ingredients
- Non-contraceptive benefits of OCs include reduced risk of ovarian and endometrial cancer, lower incidence of ectopic pregnancy and benign breast disease, increased hemoglobin levels, more regular menstrual cycles, reduced dysmenorrhea and menorrhagia, and improved hirsutism and acne
- The Centers for Disease Control and Prevention (CDC) recommend COCs and progestin-only OCs as effective methods of contraception

# Contraceptives

- Details on the appropriate selection of an effective contraceptive method are described in CDC's published Medical Eligibility Criteria
- The CDC also provides guidance to improve family planning services in the U.S., including the use of contraceptives
- The American College of Obstetricians and Gynecologists (ACOG) confirm the Medical Eligibility Criteria and recommend appropriate use of the criteria for women with co-existing medical conditions who need contraception
- ACOG also released an opinion statement in favor of OTC access for OCs without regard to age, stating that women are capable of self-screening and determining their own eligibility for OCs

# Contraceptives

- 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
- 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

# Contraceptives

- The use of OCs is associated with increased risks of serious conditions, including MI, thromboembolism, stroke, retinal thrombosis, glucose intolerance, hypertension, hepatic tumors, and gallbladder disease
- Risk of serious morbidity or mortality is very small in healthy women, but underlying risk factors can increase that risk
- Various oral, injectable, and intrauterine progestin-only OC products have been found to have no significant elevated risk of VTE, MI, stroke, or hypertension

# Contraceptives

## *Product/Guideline Updates*

- FDA has approved Miudella for prevention of pregnancy in females of reproductive potential for up to 3 years. It is available through a restricted program called the Miudella REMS Program
- FDA approved proprietary name change from Phexxi to Phexx
- Teva will discontinue brand name Ocella. Several other drospirenone/ethinyl estradiol products remain on the market
- Teva will discontinue brand name Yasmin tablet kit. Several other drospirenone/ethinyl estradiol products remain on the market

# Hypoglycemics, DPP4s

ARIZONA
HEALTH CARE COST
CONTAINMENT SYSTEM

| Drug | Manufacturer | Indications |
|---|---|---|
| **Dipeptidyl Peptidase-4 (DPP-4) Enzyme Inhibitors** | | |
| alogliptin (Nesina®) | Takeda, Perrigo/Padagis | ▪ Adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus (T2DM) |
| alogliptin/metformin (Kazano®) | Takeda, Perrigo/Padagis | |
| alogliptin/pioglitazone (Oseni®) | Takeda, Perrigo/Padagis | |
| linagliptin (Tradjenta®) | Boehringer Ingelheim | ▪ Adjunct to diet and exercise to improve glycemic control in adults with T2DM |
| linagliptin/empagliflozin (Glyxambi®)<br><br>linagliptin/empagliflozin/metformin ER (Trijardy® XR) | Boehringer Ingelheim | ▪ Adjunct to diet and exercise to improve glycemic control in adults with T2DM<br>▪ Empagliflozin is indicated to reduce the risk of cardiovascular death in adults with T2DM and established cardiovascular disease (CVD) |

| Drug | Manufacturer | Indications |
|---|---|---|
| linagliptin/metformin (Jentadueto®) | Boehringer Ingelheim | ▪ Adjunct to diet and exercise to improve glycemic control in adults with T2DM when treatment with both linagliptin and metformin is appropriate |
| linagliptin/metformin ER (Jentadueto® XR) | | |
| saxagliptin (Onglyza®) | generic, AstraZeneca | ▪ Adjunct to diet and exercise to improve glycemic control in adults with T2DM |
| saxagliptin/dapagliflozin (Qtern®) | AstraZeneca | |
| saxagliptin/metformin ER (Kombiglyze® XR) | generic, AstraZeneca | ▪ Adjunct to diet and exercise to improve glycemic control in adults with T2DM when treatment with both saxagliptin and metformin is appropriate |
| sitagliptin (Januvia®) | Merck Sharp & Dohme | ▪ Adjunct to diet and exercise to improve glycemic control in adults with T2DM |
| sitagliptin (Zituvio™) | Zydus | |
| sitagliptin/ertugliflozin (Steglujan™) | Merck Sharp & Dohme | ▪ Adjunct to diet and exercise to improve glycemic control in adults with T2DM when treatment with both ertugliflozin and sitagliptin is appropriate |
| sitagliptin/metformin (Janumet®) | Merck Sharp & Dohme | ▪ Adjunct to diet and exercise to improve glycemic control in adults with T2DM when treatment with sitagliptin and metformin is appropriate |
| sitagliptin/metformin ER (Janumet XR®) | Merck Sharp & Dohme | ▪ Adjunct to diet & exercise to improve glycemic control in adults with T2DM when treatment with both sitagliptin & metformin ER is appropriate |

# Hypoglycemics, DPP4s

- It is estimated that over 38.4 million people in the U.S. have DM
- Type 2 diabetes (T2DM) accounts for over 96% of all diagnosed cases of DM
- HbA1c improvements for DPP-4s average 0.5% to 1%
- These agents are weight-neutral and have a low hypoglycemia risk when used as monotherapy or in conjunction with metformin
- DPP-4 inhibitors are administered orally and are dosed once daily

# Hypoglycemics, DPP4s

- TECOS study reported that sitagliptin has a neutral effect on CV risk
- In addition, the CARMELINA trial demonstrated non-inferiority of linagliptin (Tradjenta) to placebo in CV outcomes
- A possible slight increased risk of HF with saxagliptin and alogliptin was found in SAVOR-TIMI and EXAMINE trials, respectively
- Along with metformin, guidelines now recommend GLP-1RAs and SGLT2 inhibitors with proven benefit as first-line treatment options, particularly for patients with atherosclerotic cardiovascular disease, CKD, and HF

# Hypoglycemics, DPP4s

- DPP-4 inhibitors, insulin, sulfonylureas, thiazolidinediones (TZDs), and/or alpha-glucosidase inhibitors may be added for glycemic control, as needed
- Diabetes treatment regimens should be individualized based on factors including:
  - Need for weight loss
  - Hypoglycemia risk
  - Co-morbidities
  - Patient preference
  - Drug adverse effects
  - Drug cost

# Hypoglycemics, DPP4s

***Product/Guideline Updates***

- FDA has approved Zituvimet XR tablets as an adjunct to diet and exercise to improve glycemic control in adults with T2DM
- FDA has approved a 25 mg/mL oral solution formulation of sitagliptin (Brynovin)

# Intranasal Rhinitis Agents

ARIZONA
HEALTH CARE COST
CONTAINMENT SYSTEM

# Intranasal Rhinitis Agents

## FDA-Approved Indications

| Drug | Manufacturer | Indication(s) |
|---|---|---|
| **Nasal Corticosteroids** | | |
| beclomethasone (Qnasl®)[1] | Teva Specialty | ▪ Treatment of nasal symptoms associated with seasonal and perennial allergic rhinitis in adults and adolescents 4 years of age and older |
| budesonide OTC[2] | generic | ▪ Temporary relief of hay fever or other upper respiratory allergies, including nasal congestion, runny nose, sneezing, and itchy nose, in adults and children 6 years of age and older |
| ciclesonide (Omnaris®)[3] | Covis | ▪ Treatment of nasal symptoms of seasonal allergic rhinitis in adults and children 6 years of age and older<br>▪ Treatment of nasal symptoms of perennial allergic rhinitis in adults and children 12 years of age and older |
| ciclesonide (Zetonna®)[4] | Covis | ▪ Treatment of symptoms associated with seasonal allergic rhinitis in adult and pediatric patients 12 years of age and older.<br>▪ Treatment of symptoms associated with perennial allergic rhinitis in adult and pediatric patients 12 years of age and older. |
| flunisolide[5] | generic | ▪ Treatment of the nasal symptoms of seasonal or perennial rhinitis. |
| fluticasone furoate OTC (Flonase® Sensimist™)[6] | GlaxoSmithKline-Haleon | ▪ Temporary relief of symptoms of hay fever or other upper respiratory allergies, including nasal congestion, runny nose, sneezing, itchy nose, and itchy, watery eyes in adults and children 2 years of age and older |

# Intranasal Rhinitis Agents

| | | |
|---|---|---|
| fluticasone propionate[7] | generic | ▪ Management of nasal symptoms of perennial non-allergic rhinitis in adults and children 4 years of age and older |
| fluticasone propionate OTC (Flonase Allergy Relief®)[8] | generic, GlaxoSmithKline-Haleon | ▪ Temporary relief of symptoms of hay fever or other upper respiratory allergies, including nasal congestion, runny nose, sneezing, itchy nose, and itchy/watery eyes, in adults and children 4 years of age and older |
| fluticasone propionate (Xhance®)[9] | OptiNose | ▪ Treatment of chronic rhinosinusitis with nasal polyps in patients 18 years of age or older<br>▪ Treatment of chronic rhinosinusitis without nasal polyps in patients 18 years of age or older |
| mometasone furoate[10] | generic | ▪ Prophylaxis of nasal symptoms of seasonal allergic rhinitis in adults and children 12 years of age and older<br>▪ Treatment of chronic rhinosinusitis with nasal polyps in patients 18 years of age and older |
| mometasone furoate OTC (Nasonex® 24HR Allergy)[11] | Perrigo | ▪ Temporarily relieves these symptoms of hay fever or other upper respiratory allergies: nasal congestion, runny nose, sneezing, itchy nose |
| mometasone furoate (Sinuva®)[12] | Intersect ENT | ▪ Corticosteroid-eluting implant indicated for the treatment of chronic rhinosinusitis with nasal polyps in patients ≥ 18 years of age who have had ethmoid sinus surgery |
| triamcinolone OTC (Nasacort® Allergy 24HR)[13] | generic, Chattem | ▪ Temporary relief of symptoms of hay fever or other upper respiratory allergies, including nasal congestion, runny nose, sneezing, and itchy nose, in adults and children 2 years of age and older |

# Intranasal Rhinitis Agents

***FDA-Approved Indications (continued)***

| Drug | Manufacturer | Indication(s) |
|---|---|---|
| **Intranasal Antihistamines** | | |
| azelastine 0.1%.[14] | generic | ▪ Relief of symptoms of seasonal allergic rhinitis in adults and children 5 years of age and older<br>▪ Relief of symptoms of vasomotor rhinitis in patients 12 years of age and older |
| azelastine 0.15%.[15] | generic | ▪ Relief of symptoms of seasonal allergic rhinitis in adults and children 6 years of age and older<br>▪ Relief of symptoms of perennial allergic rhinitis in adults and children 6 years of age and older |
| azelastine OTC (Astepro® Allergy, Children Astepro Allergy).[16, 17] | generic, Bayer | ▪ Temporary relief of symptoms due to hay fever or other upper respiratory allergies including nasal congestion, runny nose, sneezing, and itchy nose in adults and children 6 years of age and older |
| olopatadine.[18] | generic | ▪ Relief of symptoms of seasonal allergic rhinitis in adults and pediatric patients 6 years of age and older |

# Intranasal Rhinitis Agents

| | | |
|---|---|---|
| **Antihistamine and Intranasal Corticosteroid Combinations** | | |
| azelastine/fluticasone propionate (Dymista®)‡[19] | generic, Meda/Mylan | ▪ Relief of symptoms of seasonal allergic rhinitis in adult and pediatric patients 6 years of age and older |
| olopatadine/mometasone (Ryaltris™)‡[20] | Hikma Specialty | ▪ Treatment of symptoms of seasonal allergic rhinitis in adult and pediatric patients 12 years of age and older |
| **Others** | | |
| ipratropium nasal spray 0.03%[21] | generic | ▪ Symptomatic relief of rhinorrhea associated with allergic and nonallergic perennial rhinitis in adults and children 6 years of age and older |
| ipratropium nasal spray 0.06%[22] | generic | ▪ Symptomatic relief of rhinorrhea associated with the common cold or seasonal allergic rhinitis in adults and children 5 years of age and older |

# Intranasal Rhinitis Agents

- The American Academy of Otolaryngology recommends the use of intranasal corticosteroids and oral antihistamines as key treatments for AR in adults and children over 2 years of age
- Intranasal antihistamines can be offered for patients with seasonal, perennial, or episodic AR, but they are associated with more frequent dosing and adverse effects
- AAAAI states that if a patient is not adequately controlled on an intranasal corticosteroid or has moderate to severe symptoms, addition of an antihistamine may be considered

# Intranasal Rhinitis Agents

- According to the AAAAI practice parameter, for intranasally administered treatment, they recommend inhaled antihistamines as first-line for SAR, intermittent AR, and nonallergic rhinitis (NAR)
- Intranasal corticosteroids are the preferred monotherapy for persistent AR (PAR)
- AAAAI suggests combination of an intranasal corticosteroid and intranasal antihistamine for moderate-to-severe cases of SAR, SAR and PAR that is resistant to monotherapy, and resistant NAR
- An alternative option for rhinorrhea that persists while on intranasal corticosteroids is the addition of intranasal ipratropium

# Intranasal Rhinitis Agents

- Intranasal corticosteroids are generally not associated with systemic adverse reactions in adults; local side effects may occur
- Intranasal corticosteroids are similar in efficacy
- Differences among these products include the number of sprays needed per day and dosing frequency
- Intranasal antihistamines offer an alternative to intranasal corticosteroids, oral antihistamines, and intranasal ipratropium for the treatment of AR
- Factors limiting use of intranasal azelastine and olopatadine include route of administration and taste perversion

# Lipotropics, Statins

ARIZONA
HEALTH CARE COST
CONTAINMENT SYSTEM

# Lipotropics, Statins

| Drug | Manufacturer |
|---|---|
| amlodipine/atorvastatin (Caduet®)[1] | generic, Pfizer/Viatris |
| atorvastatin (Atorvaliq®)*[2] | CMP |
| atorvastatin (Lipitor®)[3] | generic, Pfizer/Viatris |
| ezetimibe/simvastatin (Vytorin®)[4] | generic, Organon |
| fluvastatin[5] | generic |
| fluvastatin ER (Lescol XL®)[6] | generic, Novartis/Sandoz |
| lovastatin[7] | generic |
| lovastatin ER (Altoprev®)[8] | Covis |
| pitavastatin calcium (Livalo®)[9] | generic, Kowa |
| pitavastatin magnesium (Zypitamag®)*[10] | Medicure |

# Lipotropics, Statins

| | |
|---|---|
| pravastatin[11] | generic |
| rosuvastatin (Crestor®)[12] | generic, AstraZeneca |
| rosuvastatin (Ezallor Sprinkle™)*[13] | Sun |
| rosuvastatin/ezetimibe (Roszet®)*[14] | SCOV3†, Althera |
| simvastatin (Flolipid™)*[15] | Salerno |
| simvastatin (Zocor®)[16] | generic, Organon |

ER = extended release

*Atorvastatin oral suspension (Atorvaliq), ezetimibe/rosuvastatin (Roszet), simvastatin oral suspension (Flolipid), pitavastatin tablet (Zypitamag), and rosuvastatin (Ezallor) were approved as a New Drug Application (NDA) via the 505(b)(2) pathway. A 505(b)(2) NDA is a United States (US) Food and Drug Administration (FDA) approval pathway in which at least some of the information required for approval comes from studies not conducted by or for the applicant.[17] Some of the data used for approval of Atorvaliq, Roszet, Flolipid, Zypitamag, and Ezallor were derived from safety and efficacy data with atorvastatin (Lipitor), rosuvastatin (Crestor) and ezetimibe (Zetia®), simvastatin (Zocor), pitavastatin (Livalo), and rosuvastatin (Crestor), respectively.

† Authorized generic

# Lipotropics, Statins

## FDA-Approved Indications

| Indications | atorvastatin (Atorvaliq, Lipitor), amlodipine/ atorvastatin* (Caduet)[18,19,20] | ezetimibe/simvastatin (Vytorin)[21] | fluvastatin, fluvastatin ER (Lescol XL)[22,23] | lovastatin[24] | lovastatin ER (Altoprev)[25] |
|---|---|---|---|---|---|
| Primary hypercholesterolemia<br>▪ Heterozygous familial and nonfamilial<br>Reduce: Total-C, LDL-C, TG and ApoB<br>Increase: HDL-C | X | X | X | X | X |
| Heterozygous familial hypercholesterolemia<br>▪ pediatric | X<br>10–17 years<br>*(Lipitor and Atorvaliq only)* | X<br>10-17 years | X<br>10–16 years | X<br>10–17 years | -- |
| Mixed dyslipidemia<br>*Fredrickson Type*<br>▪ $II_a$ and $II_b$<br>Reduce: Total-C, LDL-C, TG and ApoB | X | X | X | X<br>To reduce total-C, LDL-C | X |
| Increase HDL-C | X | -- | -- | -- | X |
| Hypertriglyceridemia<br>*Fredrickson Type* IV | X | -- | -- | -- | -- |
| Primary dysbetalipoproteinemia<br>*Fredrickson Type* III | X | -- | -- | -- | -- |
| Homozygous familial hypercholesterolemia | X | X | -- | -- | -- |

ApoB = apoprotein B; ER = extended release; HDL-C = high density lipoprotein cholesterol; LDL-C = low density lipoprotein cholesterol; TG = triglycerides; Total-C = Total cholesterol

* Caduet is indicated when amlodipine and atorvastatin are both appropriate. Indications for amlodipine are hypertension, chronic stable angina, vasospastic angina, and angiographically documented coronary artery disease (CAD).

# Lipotropics, Statins

***FDA-Approved Indications (continued)***

| Indications | atorvastatin (Atorvaliq, Lipitor), amlodipine/ atorvastatin* (Caduet) | ezetimibe/simvastatin (Vytorin) | fluvastatin, fluvastatin ER (Lescol XL) | lovastatin | lovastatin ER (Altoprev) |
|---|---|---|---|---|---|
| Atherosclerosis slow progression | -- | -- | X | X | X |
| CVD<br>▪ primary prevention of coronary events | Reduces risk of MI, stroke, revascularization, angina | -- | -- | Reduces risk of MI, unstable angina, and need for coronary revascularization | Reduces risk of MI, unstable angina, coronary revascularization |
| CHD<br>▪ secondary prevention of coronary events | Reduces risk of MI, stroke in patients with T2DM without CHD;<br>Reduces risk of MI, stroke, CHF hospitalization, angina, and revascularization in CHD patients | -- | Reduces risk of coronary revascularization | -- | -- |

CVD = cardiovascular disease; CHD = coronary heart disease; CHF = congestive heart failure; ER = extended release; MI = myocardial infarction; T2DM = type 2 diabetes mellitus

* Caduet is indicated when amlodipine and atorvastatin are both appropriate. Indications for amlodipine are hypertension, chronic stable angina, vasospastic angina, and angiographically documented coronary artery disease (CAD).

# Lipotropics, Statins

*FDA-Approved Indications (continued)*

| Indications | pitavastatin (Livalo, Zypitamag)[26] | pravastatin[27] | rosuvastatin (Crestor, Ezallor Sprinkle)[28,29] | rosuvastatin/ ezetimibe (Roszet)[30] | simvastatin (Flolipid, Zocor)[31,32] |
|---|---|---|---|---|---|
| Primary hypercholesterolemia<br>▪ Heterozygous familial and nonfamilial<br>Reduce: Total-C, LDL-C, TG and ApoB | X | X | X | X† | X |
| Heterozygous familial hypercholesterolemia<br>▪ pediatric | X<br>8 years and older<br>*(Livalo only)* | X<br>8 years and older | X<br>8–17 years | -- | X<br>10–17 years |
| Mixed dyslipidemia<br>*Fredrickson Type*<br>▪ $II_a$ and $II_b$<br>Reduce: Total-C, LDL-C, TG and ApoB | -- | X | X‡ | -- | X |
| Increase HDL-C | X§ | X | X‡ | -- | X |
| Hypertriglyceridemia - *Fredrickson Type IV* | -- | X | X | -- | X |
| Primary dysbetalipoproteinemia - *Fredrickson Type III* | -- | X | X | -- | X |
| Homozygous familial hypercholesterolemia | -- | -- | X<br>7–17 years | X | X |
| Atherosclerosis<br>▪ slow progression | -- | X | X | -- | -- |

ApoB = apoprotein B; HDL-C = high density lipoprotein cholesterol; LDL-C = low density lipoprotein cholesterol; TG = triglycerides; Total-C = Total cholesterol

† Rosuvastatin/ezetimibe is approved as an adjunct to diet in patients with primary *non-familial* hyperlipidemia to reduce LDL-C

‡ Approval for rosuvastatin (Crestor) only

§ Livalo only

# Lipotropics, Statins

*FDA-Approved Indications (continued)*

| Indications | pitavastatin (Livalo, Zypitamag)[33] | pravastatin[34] | rosuvastatin (Crestor, Ezallor Sprinkle)[35,36] | rosuvastatin/ ezetimibe (Roszet)[37] | simvastatin (Flolipid, Zocor)[38,39] |
|---|---|---|---|---|---|
| CVD<br>▪ primary prevention of coronary events | -- | Reduces risk of MI, myocardial revascularization, CV mortality | Reduces risk of major adverse CV events (CV death, nonfatal MI, nonfatal stroke, revascularization) in patients without clinically evident CHD, but with multiple risk factors¶ | -- | -- |
| CHD<br>▪ secondary prevention of coronary events | -- | Reduces risk of MI, myocardial revascularization, CV mortality, stroke/TIA | -- | -- | Reduces total mortality risk by reducing CHD death, MI, stroke, and need for revascularization |

CV = cardiovascular; CVD = cardiovascular disease; CHD = coronary heart disease; MI = myocardial infarction; TIA = transient ischemic attack
¶ Ezallor Sprinkle is similarly indicated to reduce the risk of stroke, MI, and revascularization in patients without clinically evident CHD but with multiple risk factors

# Lipotropics, Statins

- The 3-hydroxy-3-methyl-glutaryl-coenzyme A (HMG-CoA) reductase inhibitors, also known as statins, are the standard treatment in lowering cholesterol levels
- All statins lower LDL-C, although to differing degrees, in a dose-related manner
- They have demonstrated clear improvements in primary and secondary prevention of CV events
- Statins have shown a decrease in the incidence of MI, stroke, need for revascularization, angina hospitalization, CV mortality, and overall mortality

# Lipotropics, Statins

- ACC/AHA emphasize lifestyle modification, including a reduced calorie diet and aerobic physical activity, as a critical component of atherosclerotic cardiovascular disease (ASCVD) risk reduction
- They no longer support a treat-to-target approach based on LDL-C goals
- Instead, they support treatment decisions based on patients' risk status
- They also recommend algorithms to estimate 10-year ASCVD risk
- The guidelines recommend use of maximally tolerated statin intensity

# Lipotropics, Statins

- High-intensity statin therapy on average lowers LDL-C by approximately ≥ 50%
- They recommend high-intensity statin therapy in patients with CCD to reduce the risk of major adverse cardiovascular events (MACE)
- Moderate-intensity statin therapy is recommended for patients who cannot tolerate or have a contraindication to a high-intensity statin

# Lipotropics, Statins

- AACE and the American College of Endocrinology (ACE) recommend aggressive lipid-modifying therapy to lower LDL-C, with statins as the drugs of choice
- They provide different LDL-C and triglyceride (TG) goals based on the individual's risk for CV events
- Target non-HDL-C and apolipoprotein B (apo B) levels are also provided
- Their algorithm recommends treatment intensification with the addition of other LDL-C lowering agents as needed to reach treatment goals

# Lipotropics, Statins

- US Preventive Services Task Force (USPSTF) recommends a statin for the *primary* prevention of CVD in adults ages 40 to 75 years with ≥ 1 CVD risk factor and an estimated 10-year calculated CVD event risk of ≥ 10%
- USPSTF states that clinicians may selectively prescribe statin therapy in adults ages 40 to 75 years with ≥ 1 CVD risk factor and an estimated 10-year calculated CVD event risk of 7.5% to < 10%
- There is insufficient evidence to adequately assess the risk versus benefits of initiating a statin in adults ≥ 76 years of age for primary prevention of CVD events and mortality

# Lipotropics, Statins

- The National Lipid Association (NLA) recommends lipid levels be used in conjunction with other ASCVD risk factors to assess overall risk
- Moderate to high-intensity statin therapy is considered first-line for patients at high or very high-risk for an ASCVD event
- The AHA advised that treatment for familial hypercholesterolemia (FH) should be based on LDL-C levels
- Initial drug monotherapy for those with FH includes high-intensity statin therapy

# Lipotropics, Statins

- The AHA/American Stroke Association (ASA) guideline recommends that patients with ischemic stroke in the absence of CHD, no sources of cardiac embolism, and with LDL-C > 100 mg/dL be prescribed atorvastatin 80 mg daily
- The addition of ezetimibe to a statin is recommended for patients with ischemic stroke or transient ischemic attack (TIA) who have not reached the goal of <70 mg/dL for LDL-C
- They also recommend the addition of a proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitor for very high-risk patients who have not reached the goal of < 70 mg/dL for LDL-C despite treatment with a statin and ezetimibe

# Lipotropics, Statins

- KDIGO updated recommendations for the evaluation, management and treatment of CKD in children and adults who are not receiving kidney replacement therapy
- Statins are recommended for adults with CKD who are ≥50 years of age and in patients with CKD aged 18-49 years with known CAD, DM, prior ischemic stroke or estimated 10-year incidence of coronary death or nonfatal MI > 10%

# Lipotropics, Statins

## *Product/Guideline Updates*

- Crestor (rosuvastatin) indication for CV risk reduction has been revised
- Indication now states that Crestor is indicated to reduce the risk of MACE (e.g., CV death, nonfatal MI, nonfatal stroke, arterial revascularization procedure) in adults with established CHD who are at increased risk of CVD based on age, high-sensitivity C-reactive protein ≥ 2 mg/L, and at least one additional CV risk factor

# Lipotropics, Statins

## *Product/Guideline Updates*

- Liptruzet (ezetimibe/atorvastatin) is now approved as an adjunct to diet to reduce elevated LDL C in adult patients with primary hyperlipidemia and in adults with heterozygous FH (HeFH)
- It is also approved as an adjunct to other lipid-lowering therapies, or alone if such treatments are unavailable, to reduce elevated LDL-C in adults with homozygous FH (HoFH)

# Lipotropics, Other

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# Lipotropics, Other

## FDA-Approved Indications

| Drug | Manufacturer | Indication(s) |
|---|---|---|
| **Adenosine Triphosphate-Citrate Lyase (ACL) Inhibitor** | | |
| bempedoic acid (Nexletol®)[1] | Esperion | ▪ As adjunct to diet and statin therapy for the treatment of primary hyperlipidemia in adults with heterozygous familial hypercholesterolemia (HeFH) or atherosclerotic cardiovascular disease (ASCVD) who require additional lowering of low-density lipoprotein cholesterol (LDL-C)<br>▪ To reduce the risk of MI and coronary revascularization in adults who are unable to take recommended statin therapy (including those not taking a statin) with: (1) established CVD, or (2) a high risk for a CVD event but without established CVD |
| **ACL Inhibitor/Cholesterol Absorption Inhibitor** | | |
| bempedoic acid/ ezetimibe (Nexlizet®)[2] | Esperion | ▪ As adjunct to diet and statin therapy for the treatment of primary hyperlipidemia in adults with HeFH or ASCVD who require additional lowering of LDL-C |
| **Angiopoietin-like 3 (ANGPTL3) Inhibitor** | | |
| evinacumab-dgnb* (Evkeeza®)[3] | Regeneron | ▪ As an adjunct to diet and exercise and other LDL-C lowering therapies to reduce LDL-C in adults and pediatric patients, aged 1 year and older, with HoFH |
| **Apolipoprotein B Synthesis Inhibitor** | | |
| lomitapide (Juxtapid®)[4] | Amryt/Chiesi | ▪ Reduction of LDL-C, total cholesterol (TC), apolipoprotein B (Apo B), and non-high-density lipoprotein cholesterol (non-HDL-C) in patients with HoFH, as an adjunct to a low-fat diet and other lipid-lowering treatments |

# Lipotropics, Other

| Bile Acid Sequestrants | | |
|---|---|---|
| cholestyramine (Questran®, Questran® Light)[5] | generic, Par | ▪ Primary hypercholesterolemia<br>▪ Relief of pruritus associated with partial biliary obstruction |
| colesevelam† (Welchol®)[6] | generic, Cosette | ▪ As adjunct to diet and exercise to reduce elevated LDL-C in adults with primary hyperlipidemia<br>▪ Reduction of LDL-C levels in boys and postmenarchal girls 10 to 17 years of age with HeFH who are unable to reach LDL-C target despite adequate trial of dietary therapy and lifestyle modifications<br>▪ Glycemic control in adults with type 2 diabetes mellitus (T2DM) |
| colestipol (Colestid®)[7,8] | generic, Pharmacia-Upjohn | ▪ Primary hypercholesterolemia |

* Limitations of use for evinacumab-dgnb (Evkeeza) include that (1) safety and effectiveness have not been established in patients with other causes of hypercholesterolemia, including those with HeFH; and (2) the effects on CV morbidity and mortality have not been determined.

† Limitations of use for colesevelam (Welchol) include that (1) it should not be used to treat type 1 diabetes mellitus or diabetic ketoacidosis; (2) its effects on CV morbidity and mortality have not been established; (3) it has not been studied in T2DM in combination with a dipeptidyl peptidase 4 (DPP4) inhibitor; (4) it has not been studied in Frederickson Type I, III, IV, and V dyslipidemias; and (5) it has not been studied in children < 10 years of age or in premenarchal girls.

# Lipotropics, Other

***FDA-Approved Indications (continued)***

| Drug | Manufacturer | Indication(s) |
|---|---|---|
| **Cholesterol Absorption Inhibitors** | | |
| ezetimibe (Zetia®)[9] | generic, Organon | ▪ As adjunct to diet to reduce elevated LDL-C in adults with primary hyperlipidemia, including HeFH (in combination with a statin, or as monotherapy when additional LDL-C lowering therapy is not possible)<br>▪ As adjunct to diet to reduce elevated LDL-C in patients ≥ 10 years of age with HeFH (in combination with a statin)<br>▪ Adjunct to diet to reduce elevated LDL-C in adults with mixed hyperlipidemia (in combination with fenofibrate)<br>▪ Reduce elevated LDL-C levels in adults and pediatric patients ≥ 10 years of age with HoFH (in combination with a statin and other LDL-C lowering therapies)<br>▪ Adjunct to diet for reduction of elevated sitosterol and campesterol in adults and pediatric patients ≥ 9 years of age with homozygous familial sitosterolemia |
| **Niacin** | | |
| niacin ER[10] | generic | ▪ Primary hyperlipidemia or mixed dyslipidemia<br>▪ Primary hyperlipidemia or patients with a history of coronary artery disease (CAD) and hyperlipidemia (in combination with a bile acid sequestrant)<br>▪ Severe hypertriglyceridemia as adjunct in patients at risk for pancreatitis<br>▪ Patients with a history of myocardial infarction (MI) and hyperlipidemia |
| niacin IR (Niacor®)[11] | Redmont, Avondale | ▪ Primary hypercholesterolemia (monotherapy or in combination with bile-acid binding resin)<br>▪ Hypertriglyceridemia, types IV and V hyperlipidemia for those who present with a risk of pancreatitis (adjunctive therapy) |

ER = extended release; IR = immediate release; ‡ Authorized generic (AG) available.

# Lipotropics, Other

***FDA-Approved Indications (continued)***

| Drug | Manufacturer | Indication(s) |
|---|---|---|
| **Fibric Acids** | | |
| fenofibrate[9] | generic | As an adjunct to diet:<br>▪ To reduce elevated LDL-C in adults with primary hyperlipidemia when use of recommended LDL-C-lowering therapy is not possible<br>▪ To treat adult patients with severe hypertriglyceridemia (TG ≥ 500 mg/dL) |
| fenofibrate (Fenoglide®)[10] | generic, Santarus | |
| fenofibrate (Lipofen®)[11] | Ani | |
| fenofibrate[12] | generic | |
| fenofibrate (Tricor®)[13] | generic, Abbvie | |
| fenofibric acid (Fibricor®)[14] | generic‡, Athena | ▪ Primary hyperlipidemia or mixed dyslipidemia in adults<br>▪ Severe hypertriglyceridemia (TG ≥ 500 mg/dL) in adults |
| fenofibric acid (Trilipix®)[15] | generic, Abbvie | ▪ Primary hyperlipidemia or mixed dyslipidemia<br>▪ Severe hypertriglyceridemia |
| gemfibrozil (Lopid®)[16] | generic, Pfizer | ▪ Hypercholesterolemia, Fredrickson type IIb (in patients without history of or symptoms of existing coronary heart disease [CHD])<br>▪ Hypertriglyceridemia, Fredrickson types IV and V hyperlipidemia |

# Lipotropics, Other

*FDA-Approved Indications (continued)*

| Drug | Manufacturer | Indication(s) |
|---|---|---|
| **Omega-3 Fatty Acids** | | |
| icosapent ethyl§ (Vascepa®)[20] | generic, Amarin | ▪ As adjunct to maximally tolerated statin therapy to reduce the risk of MI, stroke, coronary revascularization, and unstable angina requiring hospitalization in adults with elevated TG levels (≥ 150 mg/dL) and<br>– Established cardiovascular disease (CVD); or<br>– Diabetes mellitus and ≥ 2 additional risk factors for CVD<br>▪ As adjunct to diet, to reduce TG levels in adults with severe hypertriglyceridemia (TG ≥ 500 mg/dL) |
| omega-3 acid ethyl esters (Lovaza®)[21] | generic, Woodward | ▪ Treatment of hypertriglyceridemia in adults with TG ≥ 500 mg/dL |
| **Proprotein Convertase Subtilisin/Kexin Type 9 (PCSK9) Inhibitors** | | |
| alirocumab (Praluent®)[22] | Regeneron | ▪ To reduce the risk of MI, stroke, and unstable angina requiring hospitalization in adults with established ASCVD<br>▪ As adjunct to diet, alone or in combination with other LDL-C-lowering therapies (e.g., statins, ezetimibe), in adults with primary hyperlipidemia, including HeFH, to reduce LDL-C<br>▪ As an adjunct to other LDL-C-lower therapies in adults with HoFH to reduce LDL-C |
| evolocumab (Repatha®)[23] | Amgen | ▪ To reduce the risk of major adverse cardiovascular (CV) events (CV death, myocardial infarction, stroke, unstable angina requiring hospitalization, or coronary revascularization) in adults at increased risk for these events<br>As an adjunct to diet and exercise to reduce low-density lipoprotein cholesterol (LDL-C) in:<br>▪ Adults with hypercholesterolemia<br>▪ Adults and pediatric patients aged 10 years and older with HeFH<br>▪ Adults and pediatric patients aged 10 years and older with HoFH |
| **PCSK9-Directed Small Interfering Ribonucleic Acid (siRNA)** | | |
| inclisiran (Leqvio®)[24] | Novartis | ▪ As an adjunct to diet and exercise to reduce LDL-C in adults with hypercholesterolemia, including HeFH |

§ The effects of omega-3-acid ethyl esters on CV mortality and morbidity in patients with severe hypertriglyceridemia have not been determined. The effect of icosapent ethyl and omega-3-acid ethyl esters on the risk for pancreatitis in patients with severe hypertriglyceridemia has not been determined.

# Lipotropics, Other

- Each class of non-statin lipotropics provides a unique option for use in patients who cannot reach target lipid levels on statin monotherapy or who do not tolerate statins
- While there are not outcomes data for each class, their effects on lipids profiles are clearly substantiated
- The ACC and the AHA states that these agents (e.g., ezetimibe, PSCK9 inhibitors) may be added to maximally tolerated statin therapy to lower LDL-C sufficiently to reduce ASCVD event risk in individuals with primary severe elevations of LDL-C
- Per the Endocrine Society (ES), a fibrate is considered a first-line treatment for severe and very severe hypertriglyceridemia (with fasting TG levels > 500 mg/dL)

# Lipotropics, Other

- For patients with moderate to severe hypertriglyceridemia, fibrates, niacin, and omega-3 fatty acids alone or in combination with statins may be considered
- The AHA advised that initial drug monotherapy for those with FH includes high-intensity statin therapy
- If needed, the addition of ezetimibe followed by PCSK9 inhibitor, a bile acid sequestrant, or prescription strength niacin should be considered if target LDL-C is not met

# Lipotropics, Other

- Per the AACE/ACE, a fibrate, omega-3 fatty acid, or niacin can be considered for patients with hypertriglyceridemia who do not have established ASCVD or DM with ≥ 2 risk factors and are not at the TG goal of < 150 mg/dL with statin therapy
- All patients with severe hypertriglyceridemia (> 500 mg/dL) should receive a fibrate, prescription-grade omega-3 fatty acid, and/or niacin in order to decrease the potential for acute pancreatitis
- The ACC expert consensus decision pathway for the management of ASCVD risk reduction in patients with persistent hypertriglyceridemia emphasizes the necessary lifestyle interventions and consideration of fibrates and prescription-grade omega-3 fatty acids
- They also note that fibrates provide benefit as monotherapy but not when combined with statins

# Lipotropics, Other

- Bile acid sequestrants can be used in combination with statins, and are effective in lowering LDL-C and at producing a small increase in HDL-C
- Their effect on decreasing TG levels is between 0% and 25%
- Patients generally have poor compliance to bile acid sequestrants because of their side effect profile
- ACC's recommendations on bile acid sequestrants is to use only as a secondary alternative in patients intolerant to ezetimibe

# Lipotropics, Other

- Fibric acids lower TG levels and raise HDL-C levels to a greater extent than do the statins, but as a group have less favorable effects on clinical CV outcomes
- They should be considered as an alternative agent to the statins for specific lipid disorders or can be used as add-on therapy
- Gemfibrozil has demonstrated reductions in CHD risk primarily in subsets of patients with high TG, low HDL-C, and characteristics of metabolic syndrome

# Lipotropics, Other

- Niacin has been shown to reduce major coronary events
- Compared to immediate-release niacin (Niacor), niacin extended-release (ER) may increase compliance and reduce the incidence of flushing
- Over the counter (OTC) preparations of niacin may lack nicotinic acid or be associated with an increased risk of hepatotoxicity
- Ezetimibe reduces LDL-C, both when given alone and in combination with a statin
- The IMPROVE-IT study reported lower CV mortality and morbidity when ezetimibe was added to statin (simvastatin) therapy as compared to a statin alone

# Lipotropics, Other

- The ACC consensus decision pathway states HoFH patients, with or without clinical ASCVD, may be candidates for Juxtapid if unable to reach LDL-C goals despite maximally tolerated statin therapy with or without ezetimibe, a PCSK9 inhibitor, and/or bempedoic acid
- Lovaza and Vascepa reduce TG in patients with very high TGs (> 500 mg/dL)
- Vascepa contains only EPA; Lovaza contains both EPA and DHA
- A Science Advisory by the AHA states that omega-3 polyunsaturated fatty acid (PUFA) supplementation is reasonable in patients with CHD to reduce CHD-related mortality

# Lipotropics, Other

- Alirocumab (Praluent) and evolocumab (Repatha) both have demonstrated significant efficacy in LDL-C lowering
- The AHA advises that PCSK9 inhibitors can be added to high-intensity statin plus ezetimibe therapy in patients with FH when dual therapy does not result in desired LDL-C goal after 3 months of adherent therapy
- According to the AACE, PCSK9 inhibitors may be used in patients with T2DM as add-on to statins in those with clinical ASCVD who are at extreme risk
- The FOURIER and ODYSSEY OUTCOMES studies reported a 15% reduction in the composite of CV outcomes when Repatha or Praluent were added to optimal statin therapy

# Lipotropics, Other

- Bempedoic acid offers another option for those requiring additional cholesterol lowering therapy for patients who are not at goal with diet and maximally tolerated statin therapy
- Bempedoic acid carries risks for hyperuricemia and tendon rupture
- AACE/ACE recommend treatment intensification with the addition of other LDL-C lowering agents (e.g., PCSK9 inhibitors, ezetimibe, colesevelam, bempedoic acid) as needed to reach treatment goals
- The ACC states bempedoic acid can be added for patients who do not achieve LDL-C goals despite the addition of other non-statin agents

# Lipotropics, Other

- The CLEAR Outcomes trial demonstrated that bempedoic acid was associated with lower risk of MACE compared to placebo in patients who were unable or unwilling to take a statin and had or were at high risk for CVD
- Evinacumab (Evkeeza) has shown to decrease LDL-C by almost half as concomitant therapy in a phase 3 trial after 24 weeks
- The effects of evinacumab on CV morbidity and mortality have not been established
- The ACC consensus decision pathway states HoFH patients, with or without clinical ASCVD, may be candidates for evinacumab if unable to reach LDL-C goals despite maximally tolerated statin therapy with or without ezetimibe, a PCSK9 inhibitor, and/or bempedoic acid

# Lipotropics, Other

- Data from 3 placebo-controlled trials demonstrated a favorable safety profile and a significant reduction in LDL-C by 48% to 52% with inclisiran (Leqvio) versus placebo as add on to maximally tolerated statin therapy (with or without other lipid-modifying therapy)
- Data are not yet available regarding the effect of inclisiran on CV morbidity and mortality
- The ACC consensus decision pathway states inclisiran can be considered for patients with poor adherence to PCSK9 inhibitors or those who cannot self-inject

# Lipotropics, Other

***Product/Guideline Update***

- Amgen has announced that it will discontinue the manufacture of the Repatha Pushtronex System

# Ophthalmics, Glaucoma Agents

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# Ophthalmics, Glaucoma Agents

## FDA-Approved Indications

| Drug | Manufacturer | Reduction of elevated IOP in ocular hypertension | Reduction of elevated IOP in open-angle glaucoma |
|---|---|---|---|
| **Beta-blockers** | | | |
| betaxolol (Betoptic S®)[1,2] | generic, Novartis | X | X |
| carteolol[3] | generic | X | X |
| levobunolol[4] | generic | X | X |
| timolol (Betimol®)[5] | generic, Thea Pharma | X | X |
| timolol maleate (Timoptic®, Timoptic in Ocudose®)[6,7] | generic, Bausch & Lomb | X | X |
| timolol ER[8] | generic | X | X |
| timolol ER* (Timolol GFS)[9] | generic | X | X |
| timolol long-acting† (Istalol®)[10] | generic, Bausch & Lomb | X | X |

# Ophthalmics, Glaucoma Agents

| | | | |
|---|---|---|---|
| **Carbonic Anhydrase Inhibitors** | | | |
| brinzolamide (Azopt®)[11] | generic, Novartis/Sandoz | X | X |
| dorzolamide | generic | X | X |
| **Cholinesterase Inhibitor** | | | |
| echothiophate iodide† (Phospholine Iodide®)[12] | Fera | X | X |
| **Miotic, Topical** | | | |
| pilocarpine‡[13] | generic | X | X |
| **Prostaglandin Analogs** | | | |
| bimatoprost 0.01% (Lumigan®)[14] | Allergan | X | X |
| latanoprost emulsion* (Xelpros™)[15] | Sun | X | X |
| latanoprost solution (Xalatan®)[16] | generic, Viatris | X | X |
| latanoprostene bunod (Vyzulta®)[17] | Bausch & Lomb | X | X |
| tafluprost (Zioptan®)[18] | generic, AG, Thea Pharma | X | X |
| travoprost (Travatan® Z)[19] | generic, Sandoz | X | X |

# Ophthalmics, Glaucoma Agents

***FDA-Approved Indications (continued)***

| Drug | Manufacturer | Reduction of elevated IOP in ocular hypertension | Reduction of elevated IOP in open-angle glaucoma |
|---|---|---|---|
| **Rho Kinase Inhibitor** | | | |
| netarsudil (Rhopressa®)[25] | Alcon | X | X |
| **Sympathomimetics** | | | |
| apraclonidine (Iopidine®)[26] | generic, Harrow Eye | X[§] | X[§] |
| brimonidine (Alphagan P®)[27] | generic, Allergan | X | X |
| **Combination Products** | | | |
| brimonidine/brinzolamide (Simbrinza®)[28] | Alcon | X | X |
| brimonidine/timolol (Combigan®)[29] | generic, Allergan | X[‖] | X[‖] |
| dorzolamide/timolol (Cosopt®, Cosopt PF®)[30,31] | generic, Thea | X[‖] | X[‖] |
| netarsudil/latanoprost[*] (Rocklatan®)[32] | Alcon | X | X |

# Ophthalmics, Glaucoma Agents

- Over 3 million people in the U.S. suffer from glaucoma
- It is the second most common cause of permanent blindness in the U.S., and is the leading cause of blindness among Hispanics
- Open-angle glaucoma is associated with reduced flow through the trabecular meshwork and accounts for the majority of cases
- In closed-angle glaucoma, the iris is pushed forward against the trabecular meshwork, blocking fluid from escaping
- The goal of treatment is to maintain the IOP in a range at which the optic nerve head and retinal nerve fiber layer are stable

# Ophthalmics, Glaucoma Agents

- If an agent does not adequately decrease IOP, the patient can be switched to another therapy, or an additional medication can be added
- Fixed-dose combinations may potentially increase adherence and decrease exposure to preservatives
- The American Academy of Ophthalmology (AAO) guidelines state that prostaglandin analogs are the most effective drugs at lowering IOP and can be considered as initial medical therapy
- In clinical trials, prostaglandin agonists were at least as effective as agents from other classes, and frequently showed superior efficacy compared to timolol (Timolol GFS, Timoptic)

# Ophthalmics, Glaucoma Agents

- Brimonidine (Alphagan P), carbonic anhydrase inhibitors, and beta-blockers are capable of decreasing IOP by 15% to 25%
- Prostaglandin analogs achieve up to 33% reductions in IOP
- Prostaglandin analogs have also been shown to have an additive effect when used with beta blocker therapy
- Direct-acting miotics are second- or third-line therapy due to frequent administration and lower tolerability

# Ophthalmics, Glaucoma Agents

***Product/Guideline Update***

- The FDA has approved Zolymbus, indicated for reduction of elevated intraocular pressure in patients with open-angle glaucoma or ocular HTN

# Phosphate Binders

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# Phosphate Binders

## FDA-Approved Indications

| Drug | Manufacturer | Indication(s) |
|---|---|---|
| calcium acetate* | generic | To reduce serum phosphorus in adult with end stage renal disease (ESRD) |
| calcium acetate† | generic | For the reduction of serum phosphorus in adult with ESRD |
| calcium acetate (Phoslyra®)‡ | Fresenius Medical Care | To reduce serum phosphorus in adult with ESRD |
| ferric citrate (Auryxia®) | Keryx Biopharmaceuticals | For the control of serum phosphorus levels in adults with chronic kidney disease (CKD) on dialysis<br>Treatment of iron deficiency anemia in adults with CKD not on dialysis |
| lanthanum carbonate (Fosrenol®) | generic, Shire | To reduce serum phosphate in adults with ESRD |
| sevelamer carbonate (Renvela®) | generic, Genzyme | Control of serum phosphorus in patients ≥ 6 years of age with CKD on dialysis |
| sevelamer hydrochloride (Renagel®) | generic, Genzyme | For the control of serum phosphorus in adults with CKD on dialysis |
| sucroferric oxyhydroxide (Velphoro®) | Fresenius Medical Care | For the control of serum phosphorus in adults with CKD on dialysis |
| tenapanor HCl (Xphozah®) | Ardelyx | To reduce serum phosphorus in adults with CKD on dialysis as add-on therapy in patients who have an inadequate response to phosphate binders or who are intolerant of any dose of phosphate binder therapy |

* 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.[1]

# Phosphate Binders

- CKD affects approximately 37 million Americans in the U.S.
- 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 associated with increased risk of death
- All phosphate binders are considered effective in reducing serum phosphate levels
- 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 KDIGO advise that treatment of hyperphosphatemia include the reduction of dietary phosphorus, phosphate binding therapy, and removal of phosphorus by dialysis
- 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

# Proton Pump Inhibitors

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# Proton Pump Inhibitors

| Drug | Manufacturer | Duodenal Ulcer | | Pyrosis (Heartburn) | *H. pylori* eradication | GERD | Erosive Esophagitis | | Pathological hypersecretory conditions | Gastric ulcers | NSAID-induced gastric ulcers |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Treatment | Maintenance | | | | Treatment | Maintenance | | | |
| dexlansoprazole (Dexilant™)* | Takeda | -- | -- | X | -- | X | X | X | -- | -- | -- |
| esomeprazole magnesium (Nexium®; Esomep-EZS™) | generic, Astra Zeneca, Puretek | -- | -- | -- | X with amoxicillin + clarithromycin | X | X | X | X | -- | X (risk reduction) |
| esomeprazole magnesium OTC (Nexium® 24HR) | Pfizer | -- | -- | X | -- | -- | -- | -- | -- | -- | -- |
| esomeprazole strontium | Hanmi | -- | -- | -- | X with amoxicillin + clarithromycin | X | -- | -- | X | -- | X (risk reduction) |
| lansoprazole (Prevacid®) | generic, Takeda | X | X | -- | X with amoxicillin +/- clarithromycin | X | X | X | X | X | X (risk reduction, healing) |
| lansoprazole OTC (Prevacid® 24-HR) | Novartis | -- | -- | X | -- | -- | -- | -- | -- | -- | -- |

# Proton Pump Inhibitors

***FDA-Approved Indications (Adults) (continued)***

| Drug | Manufacturer | Duodenal Ulcer | | Pyrosis (Heartburn) | *H. pylori* eradication | GERD | Erosive Esophagitis | | Pathological hypersecretory conditions | Gastric ulcers | NSAID-induced gastric ulcers |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Treatment | Maintenance | | | | Treatment | Maintenance | | | |
| omeprazole (Prilosec®) | generic, Astra-Zeneca | X | -- | -- | X with clarithromycin +/- amoxicillin | X | X | X | X | X | -- |
| omeprazole magnesium OTC (Prilosec OTC®) | generic, Procter & Gamble | -- | -- | X | -- | -- | -- | -- | -- | -- | -- |
| omeprazole OTC | Dexcel | -- | -- | X | -- | -- | -- | -- | -- | -- | -- |
| omeprazole/ sodium bicarbonate (Konvomep™) | Azurity | | | | | | | | | X | |
| omeprazole/ sodium bicarbonate (Zegerid®) | generic, Santarus | X | -- | -- | -- | X | X | X | -- | X | -- |
| omeprazole/ sodium bicarbonate OTC (Zegerid® OTC) | Santarus, Merck | -- | -- | X | -- | -- | -- | -- | -- | -- | -- |
| pantoprazole (Protonix®) | generic, Wyeth | -- | -- | -- | -- | -- | X | X | X | -- | -- |
| rabeprazole (Aciphex®) | generic, Eisai | X | -- | -- | X with amoxicillin + clarithromycin | X (adults and pediatrics) | X | X | X | -- | -- |

# Proton Pump Inhibitors

- Proton pump inhibitors (PPIs) demonstrate gastric acid suppression superior to histamine-2 receptor antagonists (H2RAs)
- PPIs achieve a more rapid and sustained increase in gastric pH and are not associated with the rapid tachyphylaxis seen with H2RAs
- PPIs offer improved treatment of various acid-peptic disorders, including gastroesophageal reflux disease (GERD), peptic ulcer disease (PUD), and NSAID-induced gastropathy

# Proton Pump Inhibitors

- Guidelines recommend PPIs as first-line therapy for the treatment of severe GERD-related symptoms or erosive esophagitis (EE), as well as for healing esophagitis
- PPIs provide the most rapid symptomatic relief and heal esophagitis in the highest percentage of patients
- Patients with EE have high recurrence rates if not maintained on chronic PPI therapy
- Long-term use of PPIs for the treatment of patients with symptomatic GERD and Barrett's esophagus is also recommended

# Proton Pump Inhibitors

- Consideration of long-term PPI treatment for patients with asymptomatic Barrett's esophagus should be made as long as the dose is periodically reevaluated
- PPIs are used in conjunction with various antimicrobials for the eradication of *Helicobacter pylori*, the most common cause of PUD
- NSAID use, the second-most common cause of PUD, is largely responsible for upper gastrointestinal (GI) bleeding and perforation in the elderly

# Proton Pump Inhibitors

- PPIs are as effective as misoprostol at reducing NSAID-induced ulcer formation and are better tolerated
- PPIs are the preferred agent for acid suppression for dyspepsia
- PPIs are suggested for the management of eosinophilic esophagitis, per the American College of Gastroenterology (ACG)

# New Drug Reviews

Hind Douiki, Pharm.D.

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# New Drug Reviews

- Journavx (suzetrigine)
- Ryzneuta (efbemalenograstim alfa)
- Orlynvah (sulopenem etzadroxil/probenecid)

# Journavx (suzetrigine)

- Indicated for the treatment of moderate to severe acute pain in adults
- Starting 12 hours after the initial dose of 100 mg, take 50 mg of Journavx orally every 12 hours
- Use for the treatment of acute pain has not been studied beyond 14 days
- Available as a 50 mg tablet
- Contraindication: Concomitant use with strong CYP3A inhibitors
- Warning: Moderate and Severe Hepatic Impairment

# Journavx (suzetrigine)

- Adverse reactions: Pruritus, muscle spasms, increased creatine phosphokinase, and rash
- The FDA approval of Journavx was based on evidence from three clinical trials involving 2,447 patients
- Two Phase 3 trials (NAVIGATE 1 and NAVIGATE 2) evaluated Journavx against both a placebo and an active control, hydrocodone bitartrate/acetaminophen (HB/APAP), in a randomized, double-blind fashion
- A third, open-label trial assessed safety and efficacy over a longer period

# Journavx (suzetrigine)

- The trials focused on acute pain following specific surgical procedures: abdominoplasty (Trial 1) and bunionectomy (Trial 2)
- The third trial included patients with moderate to severe acute pain from various surgical or non-surgical conditions
- In the main efficacy trials, patients received an initial 100 mg dose of Journavx, followed by 50 mg every 12 hours for 48 hours
- Patients were also allowed to use ibuprofen as a rescue medication

# Journavx (suzetrigine)

- Journavx significantly reduced pain compared to placebo in both primary trials as measured by the Time-Weighted Sum of the Pain Intensity Difference over 48 hours (SPID48)
- Median time to perceptible pain relief was 34 minutes in the abdominoplasty trial and 60 minutes in the bunionectomy trial
- Journavx was not superior to the active control HB/APAP over 48 hours

# Ryzneuta (efbemalenograstim alfa)

- Indicated to decrease the incidence of infection, as manifested by febrile neutropenia, in adult patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a clinically significant incidence of febrile neutropenia
- It is not indicated for the mobilization of peripheral blood progenitor cells for hematopoietic stem cell transplantation
- Dose is 20 mg administered subcutaneously once per chemotherapy cycle, approximately 24 hours after cytotoxic chemotherapy
- Do not administer between 14 days before and 24 hours after administration of cytotoxic chemotherapy

# Ryzneuta (efbemalenograstim alfa)

- Available as 20 mg/mL solution for injection in a single-dose prefilled syringe
- Contraindication: Patients with a history of serious allergic reactions to granulocyte stimulating factors such as efbemalenograstim alfa-vuxw, pegfilgrastim, or filgrastim products
- Warnings: Fatal splenic rupture, Acute Respiratory Distress Syndrome (ARDS), serious allergic reactions (including anaphylaxis), sickle cell crises in patients with sickle cell disorders, glomerulonephritis, thrombocytopenia, Capillary Leak Syndrome, and Myelodysplastic Syndrome (MDS) and Acute Myeloid Leukemia (AML) in Patients with breast and lung cancer

# Ryzneuta (efbemalenograstim alfa)

- Adverse reactions: Nausea, anemia, and thrombocytopenia
- The FDA approved Ryzneuta based on the results of two phase 3 international clinical trials, Study GC-627-04 (NCT02872103) and Study GC-627-05 (NCT03252431)
- Study GC-627-04 was a randomized, double-blind, placebo-controlled trial
- It included 122 female patients with metastatic or nonmetastatic breast cancer who received chemotherapy with doxorubicin 60 mg/m2 and docetaxel 75 mg/m2 every 21 days, for up to 4 cycles
- Patients were randomized to 20 mg Ryzneuta (n=83) or to placebo (n=39) during chemotherapy cycle 1, followed by 20-mg Ryzneuta in cycles 2 to 4

# Ryzneuta (efbemalenograstim alfa)

- The efficacy of Ryzneuta was based on the mean duration of grade 4 (severe) neutropenia in chemotherapy cycle 1, which was lower with Ryzneuta than with placebo
- The incidence of febrile neutropenia was also lower with Ryzneuta versus with placebo in cycle 1
- Study GC-627-05 was a multicenter, randomized, multidose, active-controlled clinical trial
- It included 393 patients with nonmetastatic (stage I-III) invasive breast cancer who received docetaxel and cyclophosphamide every 21 days for up to 4 cycles

# Ryzneuta (efbemalenograstim alfa)

- The study compared the efficacy and safety of a single subcutaneous injection of 20-mg Ryzneuta (n=197) versus 6-mg pegfilgrastim (n=196) on day 2 of each chemotherapy cycle (cycles 1-4)
- The mean days of grade 4 neutropenia in patients who received Ryzneuta did not exceed that of patients who received pegfilgrastim by >0.6 days in cycle 1 of chemotherapy
- The mean days of grade 4 neutropenia in cycle 1 were 0.2 days in the 2 arms

# Orlynvah (sulopenem etzadroxil/probenecid)

- Indicated for the treatment of uncomplicated urinary tract infections (uUTI) caused by the designated microorganisms Escherichia coli, Klebsiella pneumoniae, or Proteus mirabilis in adult women who have limited or no alternative oral antibacterial treatment options
- Limitations of Use: Orlynvah is not indicated for the treatment of:
  - Complicated urinary tract infections (cUTI) or as step-down treatment after IV antibacterial treatment of cUTI
  - Complicated intra-abdominal infections (cIAI) or as step-down treatment after IV antibacterial treatment of cIAI
- Usage to Reduce Development of Drug-Resistant Bacteria should be practiced

# Orlynvah (sulopenem etzadroxil/probenecid)

- Dosage is one tablet orally twice daily for 5 days
- Available as 500 mg sulopenem etzadroxil/500 mg probenecid tablets
- Contraindications:
    - Hypersensitivity to the components of Orlynvah (sulopenem etzadroxil and probenecid) or other betalactam antibacterial drugs
    - Known blood dyscrasias
    - Known uric acid kidney stones
    - Concomitant use with ketorolac tromethamine
- Warnings: Hypersensitivity reactions, *Clostridioides difficile*-Associated Diarrhea (CDAD), and exacerbation of gout

# Orlynvah (sulopenem etzadroxil/probenecid)

- Adverse reactions: Diarrhea, nausea, vulvovaginal mycotic infection, headache, and vomiting
- Orlynvah's FDA approval was based on two Phase 3 clinical trials, SURE-1 and REASSURE
- In SURE-1, 1660 Patients with uUTI were randomized to 5 days of Orlynvah or 3 days of ciprofloxacin
- The primary endpoint was overall success, defined as both clinical and microbiologic response at day 12
- In patients with ciprofloxacin-nonsusceptible baseline pathogens, Orlynvah was compared for superiority over ciprofloxacin

# Orlynvah (sulopenem etzadroxil/probenecid)

- In patients with ciprofloxacin-susceptible pathogens, the agents were compared for noninferiority
- In the nonsusceptible population, Orlynvah was superior to ciprofloxacin, 62.6% vs 36.0%
- In the susceptible population, Orlynvah was not noninferior to ciprofloxacin, 66.8% vs 78.6%
- The difference was driven by a higher rate of asymptomatic bacteriuria (ASB) post-treatment in patients on Orlynvah
- In the combined analysis, Orlynvah was noninferior to ciprofloxacin, 65.6% vs 67.9%

# Orlynvah (sulopenem etzadroxil/probenecid)

- REASSURE was a double-blind, randomized, controlled, noninferiority trial of 5 days of Orlynvah versus amoxicillin/clavulanate for 2214 women with uUTI
- The primary end point was overall success, defined as combined clinical cure and microbiologic eradication by day 12
- In the general population, overall success occurred in 318 of 522 (60.9%) participants treated with Orlynvah versus 260 of 468 (55.6%) participants treated with amoxicillin/clavulanate, meeting criteria for noninferiority

# Orlynvah (sulopenem etzadroxil/probenecid)

- In the population with uropathogens susceptible to amoxicillin/clavulanate, Orlynvah demonstrated statistically significant superiority, with a 61.7% success rate compared to 55.0% for amoxicillin/clavulanate
- In the primary population with a baseline uropathogen not susceptible to amoxicillin/clavulanate, success occurred in 22 of 42 (52.4%) patients treated with Orlynvah versus 17 of 25 (68.0%) patients treated with amoxicillin/clavulanate

# Break and Executive Session

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# Public Therapeutic Class Votes

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# Meeting Adjournment

## 2026 Meeting Dates:

## Jan 13

## May 19

## Oct 21

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