Prime THERAPEUTICS™

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Agenda Topics

Prime THERAPEUTICS™

Overview of Disease State

Guidelines

Indications

Dosage & Formulations

Lipotropics, Other

ANTIHYPERLIPIDEMICS : ADENOSINE TRIPHOSPHATE-CITRATE LYASE INHIBITORS
ANTIHYPERLIPIDEMICS : ANGIOPOIETIN-LIKE PROTEIN INHIBITORS
ANTIHYPERLIPIDEMICS : MICROSOMAL TRIGLYCERIDE TRANSFER PROTEIN (MTP) INHIBITOR
ANTIHYPERLIPIDEMICS : PCSK-9 INHIBITORS

Disease State Description - Lipotropics, Other

Atherosclerotic Cardiovascular Disease (ASCVD)

- Cardiovascular disease (CVD) is the leading cause of death worldwide
- ~ 80% of premature cardiovascular (CV) deaths are preventable through lifestyle and behavioral changes such as diet, exercise, and smoking cessation
- ASCVD accounts for 85% of all CV deaths and represents the largest chronic disease burden in the United States
- ASCVD is a progressive condition driven by plaque buildup in the arteries, primarily composed of low-density lipoprotein cholesterol (LDL-C)
- Hypercholesterolemia, particularly elevated LDL-C, is a key modifiable risk factor for ASCVD
- Cumulative exposure to LDL-C over time significantly increases the risk of CV events such as heart attack and stroke
- Lowering LDL-C is central to reducing major adverse cardiovascular events (MACE)

Guidelines - Lipotropics, Other

The American College of Cardiology (ACC, 2022)

- Expert Consensus Decision Pathway on the Role of Nonstatin Therapies for LDL-Cholesterol Lowering in the Management of Atherosclerotic Cardiovascular Disease Risk
- **First-line therapy:**
  - Statin therapy of appropriate intensity is recommended for reducing ASCVD risk
- **When statins are insufficient or not tolerated:**
  - Additional LDL-C lowering may be needed using nonstatin therapies
- **Initial nonstatin options:**
  - Ezetimibe or PCSK9 inhibitors
- **Inclisiran:**
  - May be considered after ezetimibe or PCSK9 inhibitor in patients:
    - Not achieving > 50% LDL-C reduction
    - LDL-C remains > 55 mg/dL despite maximally tolerated statin therapy
  - Can be added to statins and ezetimibe, but should not be used with PCSK9 inhibitors due to similar mechanisms

Lipotropics, Other

evolocumab (Repatha)

November 2024 - Indication for adults with established cardiovascular disease (CVD) was updated to include reduce major adverse cardiovascular (MACE) events

August 2025 – Indication to reduce the risk of MACE in adults have been expanded to include adults who are at increased risk for these events

FDA Indications:

- **To reduce the risk of MACE events (CV death, myocardial infarction, stroke, unstable angina requiring hospitalization, or coronary revascularization) in adults at increased risk of these events**
- As an adjunct to diet, alone or in combination with other LDL-C lowering therapies, in adults with primary hyperlipidemia, including heterozygous familial hypercholesterolemia (HeFH), to reduce LDL-C
- As an adjunct to diet and other LDL-C-lowering therapies in pediatric patients aged ≥ 10 years with HeFH, to reduce LDL-C
- As an adjunct to other LDL-C-lowering therapies in adults and pediatric patients aged ≥ 10 years with homozygous familial hypercholesterolemia (HoFH), to reduce LDL-C

Recommended Dosage:

- **Adults with established CVD or primary hyperlipidemia: 140 mg subcutaneously (SC) every 2 weeks or 420 mg SC once monthly**
- Pediatric patients aged 10 years and older with HeFH: 140 mg SC every 2 weeks or 420 mg SC once monthly
- Adults and pediatric patients aged 10 years and older with HoFH: 420 mg SC once monthly, dosage can be increased to 420 mg every 2 weeks if a clinically meaningful response is not achieved in 12 weeks

Availability:

- 140 mg/mL solution prefilled single-dose SureClick autoinjector
- 140 mg/mL solution prefilled single-dose syringe

Lipotropics, Other

inclisiran (Leqvio)

August 2025 - Indication for as an adjunct to diet and statin therapy for the treatment of adults with primary hyperlipidemia, including heterozygous familial hypercholesterolemia (HeFH), to reduce LDL-C was updated to as an adjunct to diet and exercise to reduce LDL-C in adults with hypercholesterolemia, including HeFH

FDA Indication:

- **As an adjunct to diet and exercise to reduce low-density lipoprotein cholesterol (LDL-C) in adults with hypercholesterolemia, including heterozygous familial hypercholesterolemia (HeFH)**

Recommended Dosage:

- **284 mg administered as a single subcutaneous injection initially, again at 3 months, and then every 6 months by a healthcare professional**

Availability:

- Injection: 284 mg/1.5 mL (189 mg/mL) in a single-dose prefilled syringe

Antivirals, Influenza

ANTIVIRALS : INFLUENZA AGENTS

Disease State Description – Influenza Antivirals

Influenza (flu)

- Common illness affecting most people at least once in their lifetime
- Often self-limiting, but can cause serious complications in young children, elderly, and immunocompromised individuals
- High-risk groups for influenza complications include:
  - < 2 years or ≥ 65 years old
  - Immunocompromised patients
  - Pregnant/postpartum patients
  - < 19 years old on long-term aspirin- or salicylate-containing medications
  - Extremely obese patients
  - Residents of nursing homes/other chronic care facilities
  - Patients with specific chronic diseases
- Timing of the onset, peak, and end of influenza activity varies from season to season
- Influenza season in the United States occurs in fall and winter, peaking December–February, and may last until May
- Since 2010, the Centers for Disease Control and Prevention (CDC) Advisory Committee on Immunization Practices (ACIP) recommends annual influenza vaccination for everyone ≥ 6 months old without contraindications, ideally at the beginning of flu season

Guidelines - Influenza Antivirals

Centers for Disease Control and Prevention, 2024

- The CDC recommends four antivirals for outpatient treatment of uncomplicated flu: oseltamivir (Tamiflu), zanamivir (Relenza), baloxavir (Xofluza), and peramivir (Rapivab)
  - Adamantanes (amantadine and rimantadine) are not recommended due to widespread resistance
- Start empiric antiviral treatment early for:
  - Severe, complicated, or progressive illness
  - Hospitalized patients
  - High risk individuals
- Non–high-risk outpatients may be treated based on clinical judgment, even without an office visit

Influenza Antivirals

baloxavir marboxil (Xofluza)

June 2025 – FDA approved 30 mg and 40 mg packet presentations of granules for oral suspension

FDA Indication:

- Treatment of acute uncomplicated influenza in patients ≥ 5 years of age who have been symptomatic for ≤ 48 hours and who are otherwise healthy or at high risk of developing influenza-related complications
- Post-exposure prophylaxis of influenza in patients ≥ 5 years of age following contact with an individual who has influenza

Limitation:

- Influenza viruses change over time; consider available information on drug susceptibility patterns for circulating influenza virus strains when deciding whether to use Xofluza

Availability:

- Tablets: 40 mg and 80 mg
- **For oral suspension (packets): 30 mg and 40 mg per packet in about 15-20 mL of drinking water**
- For oral suspension: 40 mg/20 mL when constituted for final concentration of 2 mg/mL

Recommended Dosage:

- **Single dose treatment as soon as possible and within 48 hours of influenza symptom onset for treatment of acute uncomplicated influenza or following contact with an individual who has influenza**
- Tablets:
  - 20 kg to < 80 kg: One 40 mg tablet
  - ≥ 80 kg: One 80 mg tablet
- **Oral Suspension Packets**
  - **15 kg to < 20 kg: One 30 mg packet**
  - **20 kg to < 80 kg: One 40 mg packet**
  - **≥ 80 kg: 80 mg (Two 40 mg packets)**
- Oral Suspension Bottles
  - < 20 kg: 2 mg/kg
  - 20 kg to < 80 kg: 40 mg (20 mL)
  - ≥ 80 kg: 80 mg (40 mL)

Influenza Antivirals

Discontinuation

- **July 2025 – oseltamivir (Tamiflu)**
  - Genentech discontinued Tamiflu 30 mg capsules
  - Tamiflu 45 mg and 75 mg capsules and 6 mg/mL oral suspension remain available
  - Generic versions of all approved formulations are still accessible

Transthyretin Agents

CARDIOVASCULAR AGENTS : TRANSTHYRETIN STABILIZERS

Disease State Description - Transthyretin Agents

Transthyretin (TTR) Amyloidosis

- Rare, progressive disease caused by misfolded transthyretin (TTR) protein aggregates
- Inherited TTR gene mutations (hereditary/variant) or spontaneous occurrence (wild-type)
- Clinical phenotypes:
  - ATTR-PN (sensorimotor polyneuropathy)
  - ATTR-CM (cardiomyopathy)
  - Mixed presentations (PN + CM)
- Progressive organ/system damage leading to functional decline, reduced quality of life, and early mortality without treatment

Guidelines - Transthyretin Agents

The American Heart Association/American College of Cardiology/Heart Failure Society of America (AHA/ACC/HFSA; 2022)

- Guideline for the management of heart failure
- Diagnosis: Genetic testing distinguishes wild-type vs. hereditary ATTR-CM
- Patients with ATTR-CM and an ejection fraction < 40% may poorly tolerate guideline-directed medical therapy (GDMT)
  - Angiotensin-converting enzyme inhibitor (ACEI), Angiotensin II Receptor Blocker (ARB), and Angiotensin Receptor Neprilysin Inhibitor (ARNI) may worsen orthostatic hypotension; beta-blockers can exacerbate symptoms
- Disease-Modifying Agents:
  - TTR Stabilizers
    - Tafamidis: approved therapy; improves CV outcomes in NYHA I–III
      - Early Initiation: prevents but does not reverse amyloid
      - No benefit in NYHA IV, severe aortic stenosis, or renal impairment (eGFR < 25 mL/minute/1.73 m^2)
    - Diflunisal (off-label; limited data)
    - Acoramidis: approved; not yet in guidelines
  - TTR Silencers: patisiran, inotersen (approved for polyneuropathy; CV trials ongoing)
  - TTR Disruptors: epigallocatechin-3-gallate (EGCG), doxycycline + tauroursodeoxycholic acid (TUDCA) (limited surrogate endpoint data; no CV outcome evidence)

Transthyretin Agents

acoramidis (Attruby)

November 2024 – FDA approved new drug for treatment of the cardiomyopathy of wild-type or variant transthyretin-mediated amyloidosis (ATTR-CM) in adults to reduce cardiovascular death and cardiovascular related hospitalization

FDA Indication:

- **Treatment of the cardiomyopathy of wild-type or variant transthyretin-mediated amyloidosis (ATTR-CM) in adults to reduce cardiovascular death and cardiovascular related hospitalization**

Warnings:

- **Adverse reaction rates from clinical trials may not reflect the rates observed in practice due to varying conditions**
- **Clinical Trials: Diarrhea and Upper Abdominal Pain**

Recommended Dosage:

- **712 mg (2 tablets) orally twice daily with or without food**
- **Swallow tablets whole; do not cut, crush, or chew**

Availability:

- **Tablets: 356 mg**

Bladder Relaxants

GENITOURINARY AGENTS : OVERACTIVE BLADDER AGENTS

Disease State Description - Bladder Relaxant Preparations

Overactive Bladder (OAB)

- Chronic and debilitating syndrome
- Characterized by increased daytime urinary frequency (complaint that micturition occurs more often during waking hours than previously deemed normal) and/or nocturia (awakening ≥ 1 times per night to void), with or without urinary incontinence
- Occurs in the absence of urinary tract infection (UTI) or other detectable diseases
- More common in women compared to men
- Increases with age (highest rates observed in elderly individuals)

Guidelines - Bladder Relaxant Preparations

American Urological Association (AUA), Society of Urodynamics (SUFU) 2024

- Guideline on the diagnosis and treatment of idiopathic overactive bladder
- Share-decision making to select the best therapy or therapies based on the patient's needs, desires, and side effect tolerance
- In patients with OAB whose symptoms do not adequately respond to monotherapy, combine one or more of the following: behavioral therapy, non-invasive therapy, pharmacotherapy, and/or minimally invasive therapies is recommended
- Non-Invasive Therapies
  - Incontinence Management (e.g., diapering, pads, liners, absorbent underwear)
  - Behavioral therapy (e.g., bladder training, bladder control strategies, fluid management, pelvic floor muscle training)
- Pharmacological Therapies
  - Recommends antimuscarinic or beta-3 adrenergic receptor agonists as monotherapy
  - Combination therapy (anti-muscarinic + beta-3 adrenergic receptor agonist) is conditionally recommended for patients unresponsive to monotherapy
- Minimally Invasive Therapies (e.g., botulinum toxin injection of bladder, sacral neuromodulation, acupuncture)
  - Offer to patients who are unable or unwilling to undergo behavioral, non-invasive, or pharmacologic therapies or have inadequate response to, or intolerable side effects from pharmacotherapy or behavioral therapy
- Invasive Therapies
  - Bladder augmentation cystoplasty or urinary diversion may be offer in severely impacted patients with OAB who have not responded to all other therapeutic options
- Indwelling Catheters
  - Only recommended when OAB therapies are contraindicated, ineffective, or no longer desired by the patient and always in the context of shared decision-making due to risk of harm

Bladder Relaxants

vibegron (Gemtesa)

December 2024 - FDA approved new indication for treatment of overactive bladder (OAB) with symptoms of urge urinary incontinence, urgency, and urinary frequency in adult males on pharmacologic treatment for Benign Prostatic Hyperplasia (BPH)

FDA Indication:

- OAB with symptoms of urge urinary incontinence, urgency, and urinary frequency in adults
- **OAB with symptoms of urge urinary incontinence, urgency, and urinary frequency in adult males on pharmacological therapy for benign BPH**

Warnings:

- Urinary Retention: If urinary retention develops, discontinue
- Angioedema: Angioedema of the face and/or larynx has been reported
- Not recommended in end-stage renal disease (ESRD) with or without hemodialysis (HD) or severe hepatic impairment

Recommended Dosage:

- **75 mg orally once daily**

Availability:

- Tablets: 75 mg

Bladder Relaxants

Discontinuation

- **February 2025 – tolterodine (Detrol, Detrol LA)**
  - Mylan discontinued Detrol and Detrol LA
  - Generics remain available

Hereditary Angioedema (HAE) Agents

HEMATOLOGICAL AGENTS : HEREDITARY ANGIOEDEMA AGENTS

Disease State Description – HAE Agents

Hereditary angioedema (HAE)

- Rare, autosomal dominant disorder
- C1 inhibitor (C1-INH) proteins help regulate inflammation and vascular permeability
- Three Types:
  - Type I: Low C1-INH levels (most common)
  - Type II: Dysfunctional C1-INH
  - Type III: Normal C1-INH; caused by other gene variants
- Leads to excess bradykinin, causing increased vascular permeability
- Results in acute attacks: laryngeal, gastrointestinal, and peripheral swelling
- Laryngeal attacks are life-threatening and require emergency treatment

Guidelines - HAE Agents

The United States HAE Association Medical Advisory Board (US HAEA MAB, 2020)

- Guidelines for management of Hereditary Angioedema
- On-Demand Treatment
  - Patients should have ≥ 2 doses available for immediate use
  - First-line options: FDA approved for use in acute attacks (ecallantide, icatibant, pdC1-INH [Berinert], recombinant C1-INH [rhC1-INH])
  - Sebetralstat not yet in guidelines
- Prophylactic Treatment
  - Short-Term Prophylaxis (STP):
    - Used before known triggers (e.g., dental procedures, stress)
    - Options: Single dose pdC1-INH, anabolic androgens; rhC1-INH (less data)
  - Long-Term Prophylaxis (LTP):
    - Individualized decision based on attack burden
    - First-line options: IV/SC pdC1-INH, lanadelumab
    - Second-line options: Anabolic androgens, antifibrinolytics (used if first-line unavailable or oral therapy preferred)
    - Garadacimab-gxii not yet in guidelines
  - Children:
    - Similar indications as adults
    - pdC1-INH preferred due to strong safety/efficacy data

HAE Agents

garadacimab-gxii (Andembry)

June 2025 – FDA approved an activated Factor XII (FXIIa) inhibitor (monoclonal antibody) for prophylaxis to prevent attacks of hereditary angioedema (HAE) in adult and pediatric patients aged 12 years and older

FDA Indication:

- **Prevent HAE attacks in adult and pediatric patients ≥ 12 years old**

Warnings:

- **Nasopharyngitis**
- **Abdominal pain**

Recommended Dosage:

- **To be administered subcutaneously by the patient or a caregiver**
- **Loading dose: 400 mg (two 200 mg injections)**
- **Maintenance dose: 200 mg once monthly**

Availability:

- **200 mg/1.2 mL solution in single-dose prefilled autoinjector**
- **200 mg/1.2 mL (167 mg/mL) solution in single-dose prefilled syringe with needle safety device**

HAE Agents

sebetralstat (Ekterly)

July 2025 – FDA approved a plasma kallikrein inhibitor for treatment of acute attacks of hereditary angioedema (HAE) in adult and pediatric patients aged 12 years and older

FDA Indication:

- **Treatment of acute attacks of HAE in adult and pediatric patients ≥ 12 years old**

Warnings:

- **Headache**

Recommended Dosage:

- **Standard dose: 600 mg (2 tablets) orally at the earliest recognition of an acute HAE attack**
- **Optional second dose: 600 mg (2 tablets) may be taken 3 hours after the first dose if symptoms persist or recur**
- **Maximum daily dose: 1,200 mg (4 tablets) in any 24-hour period**
- **Moderate hepatic impairment: Use 300 mg (1 tablet); second 300 mg dose may be taken ≥ 3 hours later if needed**
- **Severe hepatic impairment: Avoid use**

Availability:

- **Tablets: 300 mg**

HAE Agents

donidalorsen (Dawnzera)

August 2025 – FDA approved a prekallikrein-directed antisense oligonucleotide indicated for prophylaxis to prevent attacks of hereditary angioedema (HAE) in adult and pediatric patients aged 12 years and older

FDA Indication:

- **Prevent HAE attacks in adult and pediatric patients ≥ 12 years old**

Warnings:

- **Hypersensitivity reactions including anaphylaxis**

Recommended Dosage:

- **To be administered subcutaneously by the patient or a caregiver**
- **80 mg every 4 weeks**
- **80 mg every 8 weeks may also be considered**
- **Moderate to Severe Hepatic Impairment: Not recommended**

Availability:

- **80 mg/0.8 mL solution in a single-dose autoinjector**

Multiple Sclerosis (MS) Agents

MULTIPLE SCLEROSIS AGENTS :

Disease State Description - Multiple Sclerosis

Multiple Sclerosis (MS)

- Complex human autoimmune-type inflammatory disease of the central nervous system (CNS)
- Characterized by demyelination and subsequent axonal degeneration
- Symptoms:
  - Sensory disturbances (numbness, paresthesia, burning, and pain) in the limbs
  - Optic nerve dysfunction
  - Ataxia, fatigue
  - Bladder, bowel, and sexual dysfunction
  - Cognitive dysfunction (affecting 40% to 70% of MS patients, independent of physical disability)
  - Severe cases may result in partial or complete paralysis
- Progresses through distinct clinical stages, which may evolve from mild to more severe forms:
  - Clinically Isolated Syndrome (CIS): First episode of neurologic symptoms lasting ≥ 24 hours due to inflammation or demyelination; MRI evidence of brain lesions increases the risk of developing MS
  - Relapsing-Remitting MS (RRMS): Characterized by clearly defined attacks followed by remission; Most patients recover function, though not always completely (~85-90% of MS cases at onset)
  - Primary Progressive MS (PPMS): Continuous worsening without distinct relapses, though temporary plateaus or minor improvements may occur (~10% of adult cases at onset)
  - Secondary Progressive MS (SPMS): Initially follows a relapsing-remitting course, later transitioning to progressive decline with or without occasional relapses or remissions
- Relapses or “attacks” typically present sub-acutely, with symptoms developing over hours to several days, persisting for several days or weeks, and then gradually resolve

Ocrevus Zunovo (ocrelizumab and hyaluronidase-ocsq)

September 2024 - FDA approved a combination of ocrelizumab and hyaluronidase-ocsq indicated for treatment of (1) relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease in adults; and (2) primary progressive MS in adults

Warnings:

- CI: Active hepatitis B virus (HBV) infection (HBV and quantitative serum immunoglobulin screenings required before first dose)
- CI: History of life-threatening administration reactions to ocrelizumab
- Vaccination with live-attenuated or live vaccines is not recommended during treatment and after discontinuation, until B cell repletion

Recommended Dosage:

- Administration by a healthcare professional as a subcutaneous injection into the abdomen
- Has different dosage/administration instructions than IV ocrelizumab
- Pre-medicate orally with corticosteroid and an antihistamine at least 30 minutes prior to each injection
- 23 mL subcutaneous in the abdomen over approximately 10 minutes every 6 months
- Patients are required to be monitored closely during all injections and for a minimum of 1 hour after the initial injection and for a minimum of 15 minutes after subsequent injections

Availability:

- 920 mg ocrelizumab and 23,000 units hyaluronidase per 23 mL(40 mg and 1,000 units per mL) solution in a single-dose vial

Multiple Sclerosis

FDA Communication

- **January 2025 – Copaxone, Glatopa (glatiramer acetate)**
  - **Boxed Warning Added**: Risk of anaphylaxis, a potentially life-threatening allergic reaction
  - **Timing**: Can occur any time during treatment, even months or years after initiation
  - **Typical Onset**: Symptoms usually appear within 1 hour of injection
  - **Patient Education**:
    - Recognize signs/symptoms of anaphylaxis (e.g., difficulty breathing, swelling, rash)
    - Seek immediate medical attention if symptoms occur

Ophthalmics, Glaucoma Agents
Ophthalmics, Dry Eye Agents

OPHTHALMIC AGENTS : CHOLINERGIC AGONISTS

Disease State Description - Ophthalmics, Cholinergic Agonists

Presbyopia

- Age-related condition causing reduced near vision due to loss of accommodation
- Occurs despite full correction of distance refractive error
- Onset: Shortly after 40 years old and affects nearly everyone with age

American Academy of Ophthalmology, 2022

- Refractive Surgery Preferred Practice Pattern
- Nonsurgical Management
  - Eyeglasses: Reading glasses, bifocal, trifocal, progressive lenses
  - Contact Lenses: Soft or rigid gas-permeable; aspheric bifocal/multifocal designs
  - Pharmaceutical Therapy:
    - Pilocarpine HCl
    - Aceclidine not yet in guidelines
  - Monovision Strategies:
    - Traditional: One eye corrected for near, the other for distance
    - Modified: Multifocal lens in one eye, distance lens in the other
- Surgical Management
  - Corneal Inlays: Implanted devices to improve near vision
  - Intraocular Lenses (IOLs): Aspheric, multifocal, accommodative designs, or monovision IOL strategies
  - Scleral Procedures: Anterior ciliary sclerotomy or scleral expansion bands

Ophthalmics, Cholinergic Agonists

New Generic

- **May 2025 – pilocarpine**
  - FDA approved the first generic to Abbvie's Vuity 1.25% ophthalmic solution from Amneal

Ophthalmics, Cholinergic Agonists

aceclidine (Vizz)

August 2025 – FDA approved new drug for treatment of presbyopia in adults

FDA Indication:

- **Treatment of presbyopia in adults**

Warnings:

- **Blurred Vision**
  - **Temporary dim or dark vision after instillation**
  - **Do not drive or operate machinery if vision is not clear**
- **Risk of Retinal Tear/Detachment**
  - **Retinal examination prior to initiation of therapy**
  - **Seek immediate care with sudden onset of flashing lights, floaters, or vision loss**
- **Iritis**
  - **Caution is advised in patients with a history of iritis**

Recommended Dosage:

- **Instill one drop in each eye, wait 2 minutes and instill a second drop in each eye once daily**

Availability:

- **Ophthalmic solution: aceclidine 1.44% in a single-dose vial**

Macular Degeneration Agents

OPHTHALMIC AGENTS : COMPLEMENT INHIBITORS

Disease State - Ophthalmics, Complement Inhibitors

Age related macular degeneration (AMD)

- Progressive retinal disease
- Leading cause of central vision loss in patients > 50 years
- Types of AMD
  - Dry AMD (non-neovascular, nonexudative)
    - Characterized by drusen buildup and thinning of the macula
    - Can progress to geographic atrophy (GA), marked by irreversible degeneration of retinal pigment epithelium (RPE) and photoreceptor cells in the macula
  - Wet AMD (neovascular, exudative)
    - Choroidal neovascularization (CNV) develops under the retina and macula
    - Leads to faster and more severe vision loss
    - Can also result in GA in late stages

American Academy of Ophthalmology, 2024

- Age-Related Macular Degeneration Preferred Practice Pattern for Geographic Atrophy (GA) in AMD
- Age-Related Eye Disease Study 2 (AREDS2) Supplements:
  - Recommended for patients with intermediate AMD or GA in one/both eyes
  - Formulation includes: Vitamin C, Vitamin E, Lutein/Zeaxanthin, Zinc, and Copper
- FDA-Approved Intravitreal Therapies:
  - Pegcetacoplan (Syfovre) – C3 inhibitor
  - Avacincaptad pegol (Izervay) – C5 inhibitor

Ophthalmics, Complement Inhibitors

avacincaptad pegol (Izervay)

February 2025 – Dosing for treatment of geographic atrophy (GA) secondary to age-related macular degeneration (AMD) has been expanded for use beyond 12 months

FDA Indication:

- **Treatment of geographic atrophy (GA) secondary to age-related macular degeneration (AMD)**

Warnings:

- Contraindications: Ocular or periocular infections and active intraocular inflammation
- Endophthalmitis and Retinal Detachments, Neovascular AMD, Increase in Intraocular Pressure (IOP)

Recommended Dosage:

- 2 mg (0.1 mL of 20 mg/mL solution) administered by intravitreal injection to each affected eye once monthly (approximately 28 ± 7 days)

Availability:

- Intravitreal solution: 20 mg/mL in a single-dose vial

Oncology – Prostate

ONCOLOGY AGENTS : ANTIANDROGENS - ORAL

Disease State Description - Oncology – Prostate

Prostate Cancer

- Most common cancer in men in the United States (U.S.) (excluding skin cancer)
- 1 in 8 men will be diagnosed with prostate cancer during their lifetime
- More common in older men; rare in men under 40
  - 60% of cases are diagnosed in men aged 65 or older
  - Average age at diagnosis is about 67 years
- Second-leading cause of cancer death in American men (after lung cancer)
  - 1 in 44 men will die from prostate cancer
- Prostate cancer is classified as clinically localized disease, regional disease, or metastatic disease

National Comprehensive Cancer Network (NCCN) – Prostate Cancer, 2025

- **Metastatic castration-sensitive prostate cancer (mCSPC)**
  - **Category 1 Recommendations**
    - Androgen deprivation therapy (ADT) + (apalutamide, abiraterone, or enzalutamide)
    - ADT + docetaxel + (abiraterone or darolutamide): High-volume disease
  - **Other Recommendations**
    - ADT alone: For asymptomatic patients or life expectancy ≤ 5 years
    - ADT + darolutamide (Category 2B): High or low-volume disease
    - ADT + Radiation therapy (RT) +/- (abiraterone, apalutamide, docetaxel, or enzalutamide): Low-volume synchronous metastatic disease

Oncology – Prostate

darolutamide (Nubeqa)

June 2025 - FDA approved new indication for use as a single agent for treatment of adults with metastatic castration-sensitive prostate cancer (mCSPC)

FDA Indication:

- Treatment of adult patients with:
  - Non-metastatic castration-resistant prostate cancer (nmCRPC)
  - **Metastatic castration-sensitive prostate cancer (mCSPC)**
  - Metastatic castration-sensitive prostate cancer (mCSPC) in combination with docetaxel

Warnings:

- Ischemic heart disease, seizure, embryo-fetal toxicity

Recommended Dosage:

- **600 mg orally twice daily with food until disease progression or unacceptable toxicity occurs**
- **Severe Renal Impairment (not on hemodialysis) or Moderate Hepatic Impairment: 300 mg orally twice daily with food**
- mCSPC + docetaxel: Administer the first cycle of docetaxel within 6 weeks after the start of Nubeqa treatment
- Take with a gonadotropin-releasing hormone (GnRH) agonist or antagonist concurrently or should have had bilateral orchiectomy

Availability:

- Tablets: 300 mg

Oncology, Oral – Renal Cell

ONCOLOGY AGENTS : HIF-2-ALPHA INHIBITORS

Disease State Description - HIF-2-Alpha Inhibitors

Renal Cell Carcinoma (RCC)

- Most frequently diagnosed kidney cancer
- Most cases of RCC are of clear cell histology (70%)
- Classified as localized (stages I, II, and III) or advanced/metastatic (stage IV) disease

National Comprehensive Cancer Network (NCCN, 2025)

- Clinical Practice Guidelines for Kidney Cancer
- Surgical resection is preferred for Stage I–III RCC and can be curative depending on tumor location and extent
- Cytoreductive nephrectomy may benefit Stage IV patients with resectable tumors, though systemic therapy efficacy is challenging this standard
- Clear cell RCC (ccRCC)
  - First Line Treatment: Doublet therapy is standard
    - Immuno-oncology (IO) + IO: e.g., nivolumab + ipilimumab
    - IO + Tyrosine Kinase Inhibitor (TKI): e.g., pembrolizumab + axitinib, nivolumab + cabozantinib, pembrolizumab + lenvatinib
    - Choice depends on risk stratification (favorable, intermediate, poor), patient characteristics, and treatment goals
  - Subsequent Therapy
    - Depends on prior treatment:
    - If IO-naïve: options include IO-based combinations or TKIs
    - If prior IO used: options include TKIs, mechanistic Target of Rapamycin (mTOR) inhibitors, or belzutifan (HIF-2α inhibitor)

Disease State Description - HIF-2-Alpha Inhibitors

Pheochromocytoma and Paraganglioma (PPGL)

- Rare tumors that may be benign or malignant
- Pheochromocytomas form in the adrenal glands
- Paragangliomas form outside the adrenal glands, often along nerve pathways in the head, neck, and spine
- Symptoms include high blood pressure, headaches, and may be episodic or triggered
- Prognosis and treatment depend on tumor location, spread, and genetic background
- Treatment options
  - Surgery
    - Adrenalectomy is standard
    - Hormone replacement needed if both glands are removed
  - Radiation Therapy
    - External radiation or ^{131}I-MIBG for metastatic cases
  - Chemotherapy
    - Systemic, often combination therapy for advanced disease
  - Ablation Therapy
    - Radiofrequency (heat) or cryoablation (freezing) to destroy tumor cells
  - Embolization Therapy
    - Blocks blood flow to adrenal glands to kill cancer cells
  - Targeted Therapy:
    - TKIs (e.g., sunitinib, axitinib, cabozantinib) for metastatic/recurrent tumors
    - Belzutifan not yet mentioned in guidelines

HIF-2-Alpha Inhibitors

belzutifan (Welireg)

April 2025 – FDA revised indication for advanced renal cell carcinoma (RCC)

May 2025 – FDA approved a new indication for pheochromocytoma or paraganglioma (PPGL)

FDA Indication:

- Treatment of adult patients with von Hippel-Lindau (VHL) disease who require therapy for associated renal cell carcinoma (RCC), central nervous system (CNS) hemangioblastomas, or pancreatic neuroendocrine tumors (pNET), not requiring immediate surgery
- **Treatment of adult patients with advanced RCC with a clear cell component following a programmed death receptor-1 (PD-1) or programmed death-ligand 1 (PD-L1) inhibitor and a vascular endothelial growth factor tyrosine kinase inhibitor (VEGF-TKI)**
- **Treatment of adult and pediatric patients ≥ 12 years old with locally advanced, unresectable, or metastatic PPGL patients**

Warnings:

- Boxed Warning: Embryo-Fetal Toxicity
  - Verify pregnancy status prior to initiation; use effective non-hormonal contraception (may reduce hormonal contraceptives effective)
- Anemia and Hypoxia: Monitor for anemia and oxygen saturation before starting and periodically during treatment

Recommended Dosage:

- **Adults: 120 mg orally once daily**
- **Pediatrics ≥ 12 years old**
  - **≥ 40 kg: 120 mg orally once daily**
  - **< 40 kg: 80 mg orally once daily**
- **Swallow tablets whole with or without food until disease progression or unacceptable toxicity**

Availability:

- Tablets: 40 mg

Oncology, Oral – Lung

ONCOLOGY AGENTS : KRAS INHIBITORS

Disease State Description – KRAS Inhibitors

Colon Cancer

- Excluding skin cancers, colon cancer is the third most commonly diagnosed cancer, and the second leading cause of death from cancer in both men and women in the United States (US)
- Staging in colon cancer uses the TNM (tumor, node, metastases) system, which is typically employed after surgical exploration of the abdomen and pathologic examination of the surgical specimen

National Comprehensive Cancer Network (NCCN, 2025)

- Clinical Practice Guidelines for Colon Cancer
- KRAS G12C-mutated metastatic colorectal cancer (mCRC)
  - Preferred targeted therapy: (sotorasib or adagrasib) + EGFR inhibitor (cetuximab or panitumumab)
  - Monotherapy with sotorasib or adagrasib may be used if EGFR inhibitors are not tolerated
  - Use in later-line settings after progression on standard chemotherapy
  - Molecular testing for KRAS G12C should be part of initial metastatic workup

KRAS Inhibitors

sotorasib (Lumakras)

January 2025 – FDA approved new indication for KRAS G12C-mutated metastatic colorectal cancer (mCRC) in combination with panitumumab who have received prior fluropyrimidine-, oxaliplatin-, irinotecan-based chemotherapy

FDA Indication:

- As a single agent, for the treatment of adult patients with KRASG12C-mutated locally advanced or metastatic NSCLC, as determined by an FDA-approved test, who have received at least one prior systemic therapy
  - Under accelerated approval based on overall response rate (ORR) and duration of response (DOR); Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial
- **In combination with panitumumab, for the treatment of adult patients with KRAS G12C-mutated mCRC as determined by an FDA approved-test, who have received prior fluoropyrimidine-, oxaliplatin- and irinotecan-based chemotherapy**

Warnings:

- Hepatotoxicity: Monitor liver function tests every 3 weeks for the first 3 months, then once monthly as clinically indicated; Consider administering systemic corticosteroids and withhold, reduce the dose, or permanently discontinue based on severity
- Interstitial Lung Disease (ILD)/Pneumonitis: Immediately withhold if suspected; Permanently discontinue if no other causes identified

Recommended Dosage:

- **960 mg orally once daily until disease progression or unacceptable toxicity**
- **Swallow tablets whole with or without food**
- **KRAS G12C-mutated mCRC: Administer the first dose of prior to first panitumumab infusion**

Availability:

- Tablets: 320 mg, 240 mg, 120 mg

Vasopressin Receptor Antagonists

ENDOCRINE AND METABOLIC AGENTS : VASOPRESSIN RECEPTOR ANTAGONISTS - ORAL

Vasopressin Receptor Antagonists

New Generic

- **May 2025 – tolvaptan**
  - FDA approved the first generic for Otsuka's Jynarque from Lupin

Growth Hormones

ENDOCRINE AND METABOLIC AGENTS : GROWTH HORMONES

Growth Hormones

Discontinuation

- **October 2024 – somatropin (Humatrope)**
  - Lilly has discontinued Humatrope 2.88 mL injection
  - Distribution will continue through Quarter 3 and 4 of 2026, subject to market demand

GI Motility, Chronic

GASTROINTESTINAL AGENTS : IRRITABLE BOWEL SYNDROME (IBS) AGENTS / GI MOTILITY

GI Motility, Chronic

New Generic

- **January 2025 - prucalopride**
  - FDA approved the first generic for Takeda's Motegrity from Novitium

BPH Agents

GENITOURINARY AGENTS : PROSTATIC HYPERTROPHY AGENTS

Benign Prostatic Hyperplasia

Discontinuation

- **February 2025 – silodosin (Rapaflo)**
  - Abbvie discontinued Rapaflo capsules (4 mg, 8 mg)
  - The last lot in distribution expires March 2026, and the last sale date was June 2025
  - Generics remain available

New Generic

- **March 2025 – finasteride/tadalafil**
  - FDA approved a generic to Blue Water Biotech's Entadfi from Novitium

Ophthalmics - Glaucoma Agents

GLAUCOMA AGENTS : ADRENERGIC AGENTS
GLAUCOMA AGENTS : ADRENERGIC AGENTS COMBINATIONS
GLAUCOMA AGENTS : BETA - BLOCKERS
GLAUCOMA AGENTS : BETA - BLOCKERS COMBINATIONS
GLAUCOMA AGENTS : CARBONIC ANHYDRASE INHIBITORS
GLAUCOMA AGENTS : KINASE INHIBITORS
GLAUCOMA AGENTS : MIOTICS
GLAUCOMA AGENTS : PROSTAGLANDINS

Ophthalmics - Glaucoma Agents

Discontinuation

- **July 2024 – betaxolol (Betoptic S)**
  - Novartis discontinued Betoptic S ophthalmic suspension 0.25%
  - Discontinuation is not due to manufacturing, product quality, safety, or efficacy concerns
- **March 2025 – travoprost (Travatan Z)**
  - Sandoz discontinued Travatan Z 2.5 mL and 5 mL solution based on a business decision
  - Generics remain available

Idiopathic Pulmonary Fibrosis

RESPIRATORY AGENTS : PULMONARY FIBROSING AGENTS

Pulmonary Fibrosis Agents

Discontinuation

- **February 2025 – pirfenidone (Esbriet)**
  - Genentech discontinued Esbriet (pirfenidone) 267 mg capsules
  - Generics remain available

Opiate Dependence Treatments

SUBSTANCE USE DISORDER : AGENTS FOR OPIOID WITHDRAWAL
SUBSTANCE USE DISORDER : OPIOID ANTAGONISTS
SUBSTANCE USE DISORDER : OPIOID PARTIAL AGONISTS - SUBCUTANEOUS
SUBSTANCE USE DISORDER : OPIOID PARTIAL AGONISTS - TRANSMUCOSAL

Opiate Dependence Treatments

FDA Communication

- **December 2024 - buprenorphine; buprenorphine/naloxone (Suboxone; Zubsolv)**
  - FDA recommended changes to labeling for buprenorphine-containing transmucosal products for opioid dependence
  - Clarify maintenance doses can be adjusted based on therapeutic need; doses > 24 mg/day appropriate for some patients
  - New Label Suggests: “Dosages higher than 24 mg buprenorphine daily have not been investigated in randomized clinical trials but may be appropriate for some patients.”

Oncology - Breast

ONCOLOGY AGENTS : POLY (ADP-RIBOSE) POLYMERASE (PARP) INHIBITORS - ORAL

Oncology - Breast

Discontinuation

- **January 2025 - talazoparib tosylate (Talzenna)**
  - Pfizer discontinued Talzenna capsules in the strengths of 0.1 mg, 0.25 mg, 0.35 mg, 0.5 mg, 0.75 mg, and 1 mg
  - The capsule formulation is being replaced with the soft gel that is therapeutically equivalent to the original hard capsule (no change to active ingredient, strengths, administration instructions, or storage/handling)

No Significant Clinical Updates

Prime Therapeutics Market Basket	AHPDL DUR Meeting Topics
Antifungals, Topical	ANTIFUNGALS : TOPICAL
Antivirals, Other	ANTIVIRALS : SMALLPOX AGENTS
Sinus Node Inhibitor	CARDIOVASCULAR AGENTS : SINUS NODE INHIBITORS
Vasodilators, Coronary	CARDIOVASCULAR AGENTS : VASOACTIVE SOLUBLE GUANYLATE CYLCASE STIMULATORS (SGC)
Fabry's Disease	ENDOCRINE AND METABOLIC AGENTS : FABRY DISEASE AGENTS - INJECTABLE
	ENDOCRINE AND METABOLIC AGENTS : FABRY DISEASE AGENTS - ORAL
Nutrionals, Triglycerides	ENDOCRINE AND METABOLIC AGENTS : FATTY ACID METABOLISM AGENTS
Phosphate Binders	ENDOCRINE AND METABOLIC AGENTS : NH3 INHIBITORS
	GASTROINTESTINAL AGENTS : PHOSPHATE BINDER AGENTS
Hyperparathyroid Agents	ENDOCRINE AND METABOLIC AGENTS : PARATHYROID HORMONES
Uterine Disorder Treatments Pituitary Suppressive Agents	ENDOCRINE AND METABOLIC AGENTS : PITUITARY SUPPRESSANTS
UC Agents	GASTROINTESTINAL AGENTS : INFLAMMATORY BOWEL AGENTS
Stem Cell Mobilizer	HEMATOPOIETIC AGENTS : CXCR4 RECEPTOR ANTAGONISTS
Enzyme Inhibitors, Systemic	MISCELLANEOUS THERAPEUTIC CLASSES : PHOSPHOINOSITIDE 3-KINASE AGENTS
	MISCELLANEOUS THERAPEUTIC CLASSES : PIK3CA-RELATED AGENTS
	MISCELLANEOUS THERAPEUTIC CLASSES : PROGERIA TREATMENT AGENTS

Prime Therapeutics Market Basket	AHPDL DUR Meeting Topics
Potassium Binders	MISCELLANEOUS THERAPEUTIC CLASSES : POTASSIUM REMOVING AGENTS
Movement Disorders	MOVEMENT DISORDER AGENTS :
Friedreich Ataxia	NEUROMUSCULAR AGENTS : FREIDRICHS ATAXIA AGENTS
Rett Syndrome	NEUROMUSCULAR AGENTS : RETT SYNDROME AGENTS
PAH Agents, Injectable	PULMONARY HYPERTENSION AGENTS : ACTIVIN SIGNALING INHIBITOR
PAH Agents, Oral and Inhaled	PULMONARY HYPERTENSION AGENTS : COMBINATIONS
Vitamin D Preparations Hyperparathyroid	VITAMINS : VITAMIN D / VITAMIN D ANALOGS - ORAL
Hematopoietic Progenitor Cell Therapy	ONCOLOGY AGENTS : ALLOGENIC CELLULAR IMMUNOTHERAPY
Oncology, Oral- Prostate	ONCOLOGY AGENTS : GONADOTROPIN-RELEASING HORMONE (GNRH) RECEPTOR ANTAGONISTS - ORAL
Immunomodulators, Misc	ONCOLOGY AGENTS : INTERFERONS
Pituitary Suppressive Agents, LHRH	ONCOLOGY AGENTS : LHRH ANALOGS - INJECTABLE
Oncology, Oral - Other	ONCOLOGY AGENTS : GAMMA SECRETASE INHIBITORS
	ONCOLOGY AGENTS : ORNITHINE DECARBOXYLASE INHIBITORS
Chemotherapy Rescue	ONCOLOGY AGENTS : URINARY TRACT PROTECTIVE RESCUE AGENTS - ORAL

No Significant Clinical Updates

- **Antidepressants, Other**
- ANTIDEPRESSANTS : GABA RECEPTOR MODULATOR - NEUROACTIVE STEROID

- **Disease Modifiers, T1DM**
- ANTIDIABETICS : CELLULAR THERAPY

- **Cardiovascular, Other**
- CARDIOVASCULAR AGENTS : MISC

- **Pompe Disease**
- ENDOCRINE AND METABOLIC AGENTS : GAA DEFICIENCY AGENTS

- **Growth Factors**
- ENDOCRINE AND METABOLIC AGENTS : GROWTH HORMONE RELEASING HORMONES (GHRH)

- **Mucopolysaccharidosis**
- ENDOCRINE AND METABOLIC AGENTS : MUCOPOLYSACCHARIDOSIS AGENTS

- **Urea Cycle Disorders**
- ENDOCRINE AND METABOLIC AGENTS : UREA CYCLE DISORDER AGENTS - ORAL

- **Stem Cell Mobilizers**
- HEMATOPOIETIC AGENTS : STEM CELL MOBILIZERS

- **Thrombopoiesis Stimulating Proteins**
- HEMATOPOIETIC AGENTS : THROMBOPOIESIS (TPO) STIMULATING PROTEINS

- **Immunomodulators, Lupus**
- NEUROMUSCULAR AGENTS : SYSTEMIC LUPUS ERYTHEMATOSUS AGENTS

- **Ophthalmics Antiinflammatory/Immunomodulator**
- OPHTHALMIC AGENTS : IMMUNOMODULATORS

- **Smoking Cessation Agents**
- SMOKING DETERRENTS : MISC – OTHER

- **Oncology, Hematologic**
- ONCOLOGY AGENTS : HEDGEHOG PATHWAY INHIBITORS - ORAL
- ONCOLOGY AGENTS : MULTIKINASE INHIBITORS – ORAL
- ONCOLOGY AGENTS : RETINOIDS - ORAL

- **Oncology, Prostate**
- ONCOLOGY AGENTS : ANDROGEN BIOSYNTHESIS INHIBITORS - ORAL

- **Oncology, Skin**
- ONCOLOGY AGENTS : HEDGEHOG PATHWAY INHIBITORS - ORAL

- **Oncology, Renal Cell**
- ONCOLOGY AGENTS : MTOR KINASE INHIBITORS – ORAL
- ONCOLOGY AGENTS : MULTIKINASE INHIBITORS - ORAL

- **Oncology, Lung**
- ONCOLOGY AGENTS : MULTIKINASE INHIBITORS – ORAL
- ONCOLOGY AGENTS : TOPOISOMERASE INHIBITORS - ORAL

- **Oncology, Other**
- ONCOLOGY AGENTS : FGFR KINASE INHIBITORS – ORAL
- ONCOLOGY AGENTS : METHYLTRANSFERASE INHIBITORS – ORAL
- ONCOLOGY AGENTS : MULTIKINASE INHIBITORS - ORAL