Prime THERAPEUTICS™

# Washington Pharmacy Advisory Committee Meeting

August 13, 2025

Nina Huynh, PharmD, BCPS

# Agenda Topics

Prime THERAPEUTICS™

**Overview of Disease State**

**Guidelines**

**Indications**

**Dosage & Formulations**

# Stimulants & Related Agents

ADHD / ANTI-NARCOLEPSY : DOPAMINE AND NOREPINEPHRINE REUPTAKE INHIBITORS (DNRIS)
ADHD / ANTI-NARCOLEPSY : HISTAMINE H3-RECEPTOR ANTAGONIST / INVERSE AGONIST
ADHD / ANTI-NARCOLEPSY : NON-STIMULANTS
ADHD / ANTI-NARCOLEPSY : STIMULANTS - LONG ACTING
ADHD / ANTI-NARCOLEPSY : STIMULANTS - MISC
ADHD / ANTI-NARCOLEPSY : STIMULANTS - SHORT ACTING

# Disease State Description - Stimulants & Related Agents

## Attention Deficit Hyperactivity Disorder (ADHD)

- Stimulants are most used as first-line therapy for ADHD
- ADHD affects ~9.8% of children (ages 3–17) and ~2–7% of adults
- Core symptoms: inattention, hyperactivity, and impulsivity
- Often co-occurs with depression, anxiety, autism, tics, and conduct disorders
- Three main ADHD types: hyperactive, inattentive, and combined

## American Academy of Pediatrics (AAP), 2019

- **Children 4 to 5 years of age:** Recommends parent- and/or teacher-administered behavior therapy as first-line treatment
  - Methylphenidate (MPH) may be prescribed if the behavior interventions do not provide significant improvement and there continues to be moderate to severe disturbance in the child's function
- **Children 6 to 11 years of age:** Recommends FDA-approved medications for ADHD with behavioral therapy
- **Patients 12 to 18 years of age:** Recommends FDA-approved medications, with the adolescent's assent, and behavior therapy

  

# Stimulants & Related Agents

## clonidine (Onyda XR)

**May 2024 - FDA approved a new formulation of clonidine as an extended-release oral suspension for the treatment of Attention Deficit Hyperactivity Disorder (ADHD) as monotherapy or as adjunctive treatment to central nervous system (CNS) stimulant medications in pediatrics ≥ 6 years old**

**Warnings:**

- Hypotension/bradycardia: Titrate slowly and monitor vital signs frequently in patients at risk for hypotension, heart block, bradycardia, syncope, cardiovascular disease, vascular disease, cerebrovascular disease, or chronic renal failure; measure heart rate and blood pressure prior to initiation of therapy, following dose increases, and periodically while on therapy
- Somnolence/Sedation: Consider the potential for additive sedative effects with CNS depressant drugs; caution patients against operating heavy equipment or driving until they know how they respond
- Cardiac Conduction Abnormalities: May worsen sinus node dysfunction and atrioventricular (AV) block, especially in patients taking other sympatholytic drugs

**Recommended Dosage:**

- **Starting dosage: 0.1 mg orally once daily at bedtime**
- **Dose may be increased in increments of 0.1 mg per day at weekly intervals depending on clinical response**
- **Maximum dose: 0.4 mg once daily at bedtime**

**Availability:**

- **Extended-release oral suspension: 0.1 mg clonidine hydrochloride per mL**

# Stimulants & Related Agents

## Discontinuation

- **December 2024 - atomoxetine (Strattera)**
  - Eli Lilly discontinued Stattera (10 mg, 18 mg, 25 mg, 40 mg, 60 mg, 80 mg and 100 mg)
  - Generics remain available

# Disease State Description - Stimulants & Related Agents

## Hypersomnolence

- Hypersomnolence (excessive sleepiness) is the primary and often debilitating symptom experienced by patients with narcolepsy, obstructive sleep apnea-hypopnea syndrome (OSAHS), and shift work sleep disorder (SWSD)
- Defined by persistent inability to stay awake and alert for daily tasks
- Common complaints: fatigue, low energy, poor focus, disrupted sleep, snoring, and work difficulties

## The American Academy of Sleep Medicine (AASM), 2021

- Adults with narcolepsy:
  - Strongly recommends treatment with the following agents: modafinil, pitolisant, sodium oxybate, and solriamfetol
  - Conditionally suggested treatment options include armodafinil, dextroamphetamine, and methylphenidate
- Pediatric patients with narcolepsy:
  - Conditionally suggests treatment with modafinil and sodium oxybate
  - Notably, modafinil is not approved for this use in pediatric patients

## pitolisant (Wakix)

**June 2024 – FDA approved a new indication for treatment of excessive daytime sleepiness (EDS) in pediatric patients ≥ 6 years old with narcolepsy**

### FDA Indication:

- Treatment of excessive daytime sleepiness (EDS) or cataplexy in adult patients with narcolepsy
- **Treatment of excessive daytime sleepiness (EDS) in pediatric patients 6 years of age and older with narcolepsy**

### Warnings:

- CI: Severe hepatic impairment
- QT Interval Prolongation: Avoid use with drugs that also increase the QT interval and in patients with risk factors for prolonged QT interval; monitor patients with hepatic or renal impairment for increased QTc

### Recommended Dosage:

| | Adults: EDS or Cataplexy | Pediatric Patients (6 years and older): EDS |
|---|---|---|
| **Week 1** | Initiate with a dosage of 8.9 mg once daily | **Initiate with a dosage of 4.45 mg once daily** |
| **Week 2** | Increase dosage to 17.8 mg once daily | **Increase dosage to 8.9 mg once daily** |
| **Week 3** | May increase to the maximum recommended dosage of 35.6 mg once daily | **Increase dosage to 17.8 mg once daily, the maximum recommended dosage for patients < 40 kg** |
| **Week 4** | | **For patients ≥ 40 kg, may increase to the maximum recommended dosage of 35.6 mg once daily** |

### Availability:

- Oral Tablets: 4.45 mg and 17.8 mg

 

# Anti-Allergens, Oral

## ALLERGY : ALLERGENIC EXTRACTS / BIOLOGICALS - ORAL

# Disease State Description - Anti-Allergens, Oral

## Peanut Allergies

- Affect ~ 1 million children in the United States (U.S.), only 20% outgrow it
- Food allergies causes ~4–10 deaths/year in the U.S.
- Peanut allergies linked to 35 of 91 food allergy deaths (2010-2019)
- Reactions range from mild (skin or gastrointestinal symptoms) to severe (angioedema and anaphylaxis)
- Antihistamines treat mild to moderate cases; epinephrine auto-injector needed for severe reactions

# Anti-Allergens, Oral

## peanut allergen powder-dnfp (Palforzia)

**August 2024 - FDA expanded the age indication for the mitigation of allergic reactions, including anaphylaxis, that may occur from accidental exposure to peanut in patients with a confirmed peanut allergy diagnosis to include patients 1 to 17 years old for initial dose escalation and patients ≥ 1 years old for up-dosing and maintenance**

**Limitation:**

- **Not indicated for the emergency treatment of allergic reactions, including anaphylaxis**

**Warnings:**

- BBW: Anaphylaxis; only available through Palforzia REMSA
- CI: Uncontrolled asthma; history of eosinophilic esophagitis or other eosinophilic gastrointestinal disease

**Recommended Dosage:**

- **Administered in 3 sequential phases:**
  - **Initial dose escalation for ages 1 through 17: Administered by mouth on a single day by a health care professional (HCP)**
  - **Up-Dosing for ages ≥ 1 year: First dose of each new up-dosing level must be HCP-administered, titrated every 2 weeks as tolerated**
  - **Maintenance for ages ≥ 1 year: 300 mg by mouth daily**

| Patient Population | Initial Dose Escalation | Up-Dosing |
|---|---|---|
| **Ages 1 through 3** | **4 doses starting from 0.5 mg to 3 mg** | **12 levels starting at 1 mg** |
| Ages 4 through 17 | 5 doses starting from 0.5 mg to 6 mg | 11 levels starting at 3 mg |

**Availability:**

- Powder for oral administration: 0.5 mg, 1 mg, 10 mg, 20 mg, and 100 mg capsules or 300 mg sachets

# Disease State Description - Anti-Allergens, Oral

## Dust Mite Allergy

- Dust mites are a leading cause of year-round allergies and allergic asthma
- Symptoms: sneezing, congestion, postnasal drip, cough, itchy/watery eyes, and throat irritation
- Allergen avoidance and medications (e.g. antihistamines, nasal corticosteroids, leukotriene receptor antagonist, cromolyn sodium spray or decongestants) can provide symptom relief, but symptoms remain for many
- Allergen immunotherapy may be a suitable option for persistent cases

# Anti-Allergens, Oral

## house dust mite *(Dermatopagoides farinae & Dermatophagoides pteronyssinus)* allergen extract (Odactra)

**March 2025- FDA expanded the age indication for use as immunotherapy for treatment of house dust mite-induced allergic rhinitis, with or without conjunctivitis, to include pediatrics aged 5 to 11 years old**

**FDA Indication:**

- **Treatment of house dust mite (HDM)-induced allergic rhinitis, with or without conjunctivitis, confirmed by positive in vitro testing for IgE antibodies to Dermatophagoides farinae or Dermatophagoides pteronyssinus house dust mites or by positive skin testing to licensed house dust mite allergen extracts, for use in individuals 5 through 65 years of age**

**Warnings:**

- BBW: Anaphylaxis
- CI: Severe, unstable or uncontrolled asthma; history of eosinophilic esophagitis or any severe systemic allergic reaction or any severe local reaction to sublingual allergen immunotherapy

**Recommended Dosage:**

- **One tablet sublingually once daily**
- **First dose should be administered in a healthcare setting under HCP supervision**

**Availability:**

- Tablet: 12 SQ-HDM

# Antiparkinson’s Agents

ANTIPARKINSON AGENTS : ADENOSINE RECEPTOR ANTAGONISTS
ANTIPARKINSON AGENTS : DOPAMINERGICS
ANTIPARKINSON AGENTS : MONOAMINE OXIDASE INHIBITORS (MAOI)

# Disease State Description - Antiparkinson's Agents

## Parkinson's Disease (PD)

- Progressive neurodegenerative disorder with key motor symptoms: tremor, bradykinesia, rigidity, and postural/gait instability
- Affects ~1% of individuals > 60 years of age; incidence rises significantly with age
- "Parkinsonism" refers to the motor syndrome of bradykinesia, rigidity, tremor, and balance and gait disturbances
- No cure exists; symptomatic treatments help but disability progresses over time

## American Academy of Neurology (AAN, 2021)

- Reaffirmed February 8, 2025
- Levodopa as the preferred initial treatment for motor symptoms in early PD (Level B)
- Dopamine agonists may be used for patients < 60 years old at higher risk for the development of dyskinesia (Level C)
- Avoid dopamine agonists in patients with higher risk of medication-related adverse effects (> 70 years of age, history of impulse control disorders, pre-existing cognitive impairment, excessive daytime sleepiness (EDS), or hallucinations) (Level B)
- Immediate-release levodopa is recommended over controlled-release levodopa or levodopa/carbidopa/entacapone (Level B)
- Long-acting forms of levodopa and levodopa with entacapone do not appear to differ in efficacy from immediate-release levodopa for motor symptoms in early disease

# Antiparkinson's Agents

## carbidopa / levodopa (Crexont)

**August 2024 – FDA approved a new formulation of carbidopa and levodopa combination as an extended-release capsule for the treatment of Parkinson's disease, post-encephalitic parkinsonism, and parkinsonism that may follow carbon monoxide intoxication or manganese intoxication in adults**

**Warnings:**

- CI: Nonselective monoamine oxidase (MAO) inhibitors
- Cardiovascular events, hallucinations, psychosis, impulse control disorder, dyskinesia, and falling asleep during activities of daily living
- Pregnancy: Based on animal data, may cause fetal harm
- Withdrawal-emergent hyperpyrexia and confusion: Avoid sudden discontinuation or rapid dose reduction

**Recommended Dosage:**

- **Levodopa-naïve patients:**
  - **Starting dose: 35 mg carbidopa/140 mg levodopa orally twice daily for the first 3 days**
  - **Increase dose gradually as needed**
- **Patients converting from immediate-release (IR):**
  - **Not substitutable on a 1:1 basis with immediate-release carbidopa/levodopa**
  - **Starting dose: Based on total daily and most frequent single immediate-release levodopa dosage**
  - **Adjust dose or frequency after one to three days based on patient's clinical response and tolerability as needed**
- **Maximum daily dose: 525 mg carbidopa/2,100 mg levodopa divided up to 4 times daily**

**Availability:**

- **Extended-Release Capsules: Carbidopa and Levodopa 35 mg/140 mg, 52.5 mg/210 mg, 70 mg/ 280 mg, 87.5 mg/350 mg**

# Antiparkinson's Agents

## foscarbidopa / foslevodopa (Vyalev)

**October 2024 - FDA approved a combination of foscarbidopa and foslevodopa for treatment of motor fluctuations in adults with advanced Parkinson's disease**

**Warnings:**

- **CI: Nonselective monoamine oxidase (MAO) inhibitors**
- **Hallucinations, psychosis, impulse control disorder, dyskinesia, infusion site reactions and infections, and falling asleep during activities of daily living**
- **Pregnancy: Based on animal data, may cause fetal harm**
- **Withdrawal-emergent hyperpyrexia and confusion: Avoid sudden discontinuation or rapid dose reduction**

**Recommended Dosage:**

- **Administered via subcutaneous infusion using a Vyafuser pump**
- **Continuous infusion rate is based on total levodopa dosage**
- **Maximum daily dosage: 3,525 mg of foslevodopa (equivalent to ~2,500 mg levodopa)**
- **Optional loading dose can be administered if therapy is initiated in an "off" state or patient has not been receiving base continuous infusion for > 3 hours**

**Availability:**

- **Injection: 120 mg foscarbidopa and 2,400 mg foslevodopa per 10 mL (12 mg foscarbidopa and 240 mg foslevodopa per mL)**

# Antiparkinson's Agents

## apomorphine (Onapgo)

**February 2025 – FDA approved a new formulation of apomorphine for the treatment of motor fluctuations in adults with advanced Parkinson's disease**

**Warnings:**

- CI: Concomitant use with $5HT_3$ antagonists and sulfite
- Nausea, vomiting, hypotension, orthostatic hypotension, syncope, increase risk of falls, hallucinations and psychotic-like behavior, dyskinesia, hemolytic anemia, impulse control, compulsive and impulsive behaviors, cardiac events, prolong QTc, torsades de points, or sudden death, infection site reactions and infections, and falling asleep during activities of daily living and daytime somnolence
- Pregnancy: Based on animal data, may cause fetal harm

**Recommended Dosage:**

- **Administered by continuous subcutaneous infusion only**
- **Individually titrated; includes continuous and as-needed extra doses, not exceeding 98 mg/day over the waking day (e.g., 16 hours)**
  - **Initial Infusion: Start at 1 mg/hr, titrate by 0.5 to 1 mg/hr as needed to a maximum of 6 mg/hr**
  - **Extra doses: Titrate by 0.5 to 1 mg, up to 2 mg per dose, maximum of 3 extra doses/day, spaced ≥ 3 hours apart**
- **Trimethobenzamide is recommended 3 days before the first dose of Onapgo and continue as needed to control nausea and vomiting (typically ≤ 2 months)**
- **Not a substitute for apomorphine products intended for intermittent use**
- **Mild or moderate renal impairment: Initial extra dose is 0.5 mg to 1 mg and should not exceed 1 mg**

**Availability:**

- **Injection: 98 mg/20 mL (4.9 mg/mL) of apomorphine hydrochloride in single-dose cartridges**

# Antiparkinson's Agents

## apomorphine (Apokyn)

**February 2025 - FDA approved Apokyn NXT, a new 30 mg/3 mL (10 mg/mL) single-patient-use disposable prefilled pen**

**FDA Indication:**

- Acute, intermittent treatment of hypomobility, "off" episodes ("end-of-dose wearing off" and unpredictable "on/off" episodes) associated with advanced Parkinson's disease

**Warnings:**

- CI: Concomitant use with 5HT3 antagonists and sodium metabisulfite
- Nausea, vomiting, hypotension, orthostatic hypotension, syncope, hallucinations and psychotic-like behavior, dyskinesia, hemolytic anemia, impulse control, compulsive and impulsive behaviors, cardiac events, prolong QTc, torsades de points, or sudden death, and falling asleep during activities of daily living and daytime somnolence
- Pregnancy: Based on animal data, may cause fetal harm

**Recommended Dosage:**

- Administered by subcutaneous injection; initial dose and dose titrations by HCP
- Starting dose of 0.1 mL (1mg) to 0.2 mL (2 mg), titrate up to a maximum dose of 0.6 mL
- Trimethobenzamide is recommended 3 days before the first dose of Apokyn and continue as needed to control nausea and vomiting (typically ≤ 2 months)
- Mild or moderate renal impairment: Reduce test dose and starting dose to 0.1 mL (1 mg)

**Availability:**

- Injection: 30 mg/3 mL (10 mg/mL) of apomorphine hydrochloride solution as:
  - Apokyn single-patient-use cartridges
  - **Apokyn NXT single-patient-use disposable prefilled pen**

# Antipsychotics

ANTIPSYCHOTICS / ANTIMANIC AGENTS : ANTIPSYCHOTICS - 2ND GENERATION
ANTIPSYCHOTICS / ANTIMANIC AGENTS : ANTIPSYCHOTICS - COMBINATIONS
ANTIPSYCHOTICS / ANTIMANIC AGENTS : PARKINSONS PSYCHOTIC DISORDER

# Disease State Description - Antipsychotics

## Schizophrenia

- Most common psychotic illness; affects ~1% of the population
- 20% to 40% of schizophrenic patients attempt suicide, and 4 to 5% succeed
- Symptoms are categorized as positive, negative, cognitive, and mood
- Symptoms include delusions, hallucinations, disorganized speech, disorganized or catatonic behavior

## Department of Veterans Affairs/Department of Defense (VA/DoD, 2023)

- **Acute or first-episode psychosis**: Recommends a non-clozapine antipsychotic based on individualized evaluation that considers patient characteristics and side effect profiles of the different antipsychotic medications
- **Maintenance treatment of schizophrenia**: Recommends an antipsychotic medication to prevent relapse and hospitalization in individuals with schizophrenia who have responded to treatment based on individualized evaluation that considers patient-specific characteristics and side effect profiles of the different antipsychotic medications
- **Non-response or Intolerance:** Suggest a trial of another antipsychotic medication
- **Improving adherence:** Suggest long-acting injectable antipsychotics
- **Treatment-Resistant Schizophrenia:** Recommends clozapine

## paliperidone palmitate (Erzofri)

**July 2024 – FDA approved a new formulation of paliperidone palmitate as an injectable suspension for treatment of schizophrenia in adults and schizoaffective disorder in adults as monotherapy and as an adjunct to mood stabilizers or antidepressants**

### Warnings:

- BBW: Increased Mortality in Elderly Patient with Dementia-Related Psychosis
- Neuroleptic malignant syndrome, QT prolongation, tardive dyskinesia, metabolic changes, orthostatic hypotension and syncope, leukopenia, neutropenia, agranulocytosis, hyperprolactinemia, cognitive and motor impairment, and seizures
- Pregnancy: May cause extrapyramidal and/or withdrawal symptoms in neonates with third trimester exposure

### Recommended Dosage:

- **Naïve to oral or injectable paliperidone, or oral or injectable risperidone: Establish tolerability with oral paliperidone or oral risperidone prior to initiating treatment with Erzofri**
- **Administered as a monthly intramuscular (IM) injection by an HCP**
- **Schizophrenia: 351 mg on day 1, then 39 mg to 234 mg monthly**
- **Schizoaffective disorder: 351 mg on day 1, then 78 mg to 234 mg monthly**
- **Mild renal impairment: 234 mg on day, then 78 mg to 156 mg monthly**
- **Moderate or severe renal impairment: Not recommended**

### Availability:

- **Extended-release injectable suspension: 39 mg/0.25 mL, 78 mg/0.5 mL, 117 mg/0.75 mL, 156 mg/mL, 234 mg/1.5 mL, 51 mg/2.2 mL**

 

# Octreotides & Related Agents

## ENDOCRINE AND METABOLIC AGENTS : SOMATOSTATIC AGENTS

# Disease State Description - Octreotides & Related Agents

## Carcinoid Syndrome

- Carcinoid syndrome is a term usually applied to a constellation of symptoms that arises when carcinoid tumors release excess hormones into the blood stream
  - Most commonly causes symptoms are flushing and diarrhea
- Carcinoid syndrome occurs in < 10% of patients with carcinoid tumors, usually after the tumor has spread to the liver
- Carcinoid tumors are relatively rare in the United States (US), with ~ 1.5 to 1.9 clinical cases per 100,000 people
  - Incidence is on the rise (probably related to better detection methods)

## National Comprehensive Cancer Network (NCCN) Guidelines-Neuroendocrine and Adrenal Tumors, 2022

- Somatostatin analogs for control of symptoms and tumor growth: Patients who have metastatic neuroendocrine tumors and carcinoid syndrome should be treated with a somatostatin analog (i.e., octreotide or lanreotide)
- Symptomatic patients with unresectable disease, those who initially present with clinically significant tumor burden, or those with clinically significant disease progression: Octreotide or lanreotide should be considered if patients are not already receiving these treatments

# Octreotides & Related Agents

## lanreotide

**September 2024 – FDA approved a new indication for treatment of adults with carcinoid syndrome; when used, it reduces the frequency of short-acting somatostatin analog rescue therapy**

**FDA Indication:**

- Long-term treatment of acromegalic patients who have had an inadequate response to or cannot be treated with surgery and/or radiotherapy
- Treatment of adult patients with unresectable, well- or moderately differentiated, locally advanced or metastatic gastroenteropancreatic neuroendocrine tumors (GEP-NETs) to improve progression-free survival
- **Treatment of adults with carcinoid syndrome; when used, reduces the frequency of short-acting somatostatin analog rescue therapy**

**Warnings:**

- Cholelithiasis, hyperglycemia, hypoglycemia, decrease heart rate, thyroid function abnormalities, steatorrhea and malabsorption of dietary fats

**Recommended Dosage:**

- **Administered via deep subcutaneous injection by an HCP only**
- Acromegaly: 90 mg every 4 weeks for 3 months; adjust thereafter based on GH and/or IGF-1 levels regimen
- GEP-NETs: 120 mg every 4 weeks
- **Carcinoid Syndrome: 120 mg every 4 weeks**
  - **If treated with lanreotide injection for GEP-NET: Do not administer an additional dose for carcinoid syndrome**

**Availability:**

- Injection: 60 mg/0.2 mL, 90 mg/0.3 mL, and 120 mg/0.5 mL of lanreotide in single-dose prefilled syringes

# Bile Salts

## GASTROINTESTINAL AGENTS : ILEAL BILE ACID TRANSPORTER INHIBITORS

# Disease State Description - Bile Salts

## Progressive Familial Intrahepatic Cholestasis (PFIC)

- Rare, autosomal recessive, heterogeneous group of disorders resulting in impaired bile flow due to impaired bile acid (BA) secretion leading to cholestatic liver injury
- The disease presents in early childhood with pruritus, elevated liver tests, jaundice, and growth failure
- ~ 400-500 patients with PFIC in the U.S.
- Generally, the treatment of choice for pruritus associated with cholestasis is correction of the underlying hepatobiliary disease, when possible
  - If the underlying hepatobiliary disease cannot be corrected, treatment is aimed at the pruritus itself

# Bile Salts

## maralixibat (Livmarli)

**July 2024 – FDA expanded the indication age for treatment of cholestatic pruritis in patients with progressive familial intrahepatic cholestasis (PFIC) to include patients ≥ 12 month of age**

**April 2025 - FDA approved new dosage forms of 10 mg, 15 mg, 20 mg, and 30 mg oral tablets**

### FDA Indication:

- Treatment of cholestatic pruritus in patients 3 months of age and older with Alagille syndrome (ALGS)
- **Treatment of cholestatic pruritus in patients 12 months of age and older with PFIC**

### Limitation:

- **Not recommended in a subgroup of PFIC type 2 patients with specific ABCB11 variants resulting in nonfunctional or complete absence of bile salt export pump (BSEP) protein**

### Warnings:

- Contraindicated: Prior or active hepatic decompensation events (e.g., variceal hemorrhage, ascites, hepatic encephalopathy)
- Hepatotoxicity, gastrointestinal adverse reactions, fat-soluble vitamin (FSV) deficiency, propylene glycol toxicity (patients < 5 years of age)

### Recommended Dosage:

| Indication | Recommended Dose | Starting Dose | Titration | Maximum daily dose |
|---|---|---|---|---|
| ALGS | 380 mcg/kg once daily, taken 30 minutes before the morning meal | 190 mcg/kg orally once daily | Increase to 380 mcg/kg once daily after one week, as tolerated | 28.5 mg (oral solution)<br>**30 mg (tablet)** |
| PFIC | **570 mcg/kg twice daily, taken 30 minutes before a meal** | **285 mcg/kg orally once daily in the morning** | **Increase to 285 mcg/kg twice daily, 428 mcg/kg twice daily, and then to 570 mcg/kg twice daily, as tolerated** | **38 mg (oral solution)**<br>**40 mg (tablet)** |

### Availability:

- Oral solution: 9.5 mg of maralixibat per mL for treatment of ALGS, **19 mg of maralixibat per mL for treatment of PFIC**
- **Tablets: 10 mg, 15 mg, 20 mg, and 30 mg (ALGS or PFIC in patients ≥ 25 kg)**

# Paroxysmal Nocturnal Hemoglobinuria (PNH) Agents

## HEMATOLOGICAL AGENTS : COMPLIMENT INHIBITORS - INJECTABLE

# Disease State Description – PNH Agents

## Paroxysmal Nocturnal Hemoglobinuria (PNH)

- Rare hematologic disorder characterized by complement mediated hemolysis resulting in anemia, hemoglobinuria, and complications related to presence of free hemoglobin
- Affects both men and women at any age
- ~ 0.6 to 6.1 cases per million people in the United States (US)
- Treatments: Supportive care, allogeneic hematopoietic stem cell transplant (HSCT), and complement inhibitors

## Atypical hemolytic uremic syndrome (aHUS)

- Ultra-rare disease characterized by acute kidney injury, thrombocytopenia, and microangiopathic hemolytic anemia
- Caused by uncontrolled complement activation leading to thrombotic microangiopathy (CM-TMA)
- Can progress to cause kidney failure, heart disease and other serious health problems
- First-line Treatments: Complement inhibitors (eculizumab, ravulizumab) have been shown to maintain glomerular perfusion and function

# Disease State Description – PNH Agents

## Myasthenia Gravis (MG)

- Relatively uncommon, but the most common disorder of neuromuscular transmission
- Caused by an antibody-mediated attack of the proteins in the postsynaptic membrane of the neuromuscular junction
- **Cardinal features:** fluctuating skeletal muscle weakness, often with true muscle fatigue
- **Clinical forms:**
  - **Ocular MG:** Weakness is limited to the eyelids and extraocular muscles
  - **Generalized MG (gMG):** Weakness may involve ocular muscles, bulbar, limb, and respiratory muscles
- **Treatment options**:
  - First line: Cholinesterase inhibitors (e.g. pyridostigmine) for managing symptoms
  - Immunosuppressants (azathioprine, mycophenolate mofetil), glucocorticoids, or rituximab may elicit a response in patients, depending upon the MG subtype
  - Treatment of severe, refractory, acetylcholine receptor antibody positive (AChR-Ab+) gMG: Eculizumab

# PNH Agents

## crovalimab-akkz (Piasky)

**June 2024 – FDA approved s new drug for treatment of adult and pediatric patients ≥ 13 years old with paroxysmal nocturnal hemoglobinuria (PNH) and body weight of ≥ 40 kg**

**Warnings:**

- **BBW: Risk of Serious Meningococcal Infections; only available through Piasky REMS program**
  - **Complete meningococcal vaccine ≥ 2 weeks before starting unless risks of delaying therapy outweigh risks of developing serious infection**
  - **Contraindicated for initiation in patients with unresolved serious *Neisseria meningitidis* infections**

**Recommended Dosage:**

- **Based on patient's actual body weight**
- **Loading doses: 1 intravenous infusion, followed by 4 additional loading doses administered by subcutaneous injection**
- **Maintenance doses: Every 4 weeks by subcutaneous injection**
- **Switching from another complement inhibitor: First loading dose of Piasky should be administered no sooner than the time of the next scheduled complement inhibitor administration**

**Availability:**

- **Injection: 340 mg/2 mL (170 mg/mL) in a single-dose vial**

# PNH Agents

## eculizumab-aeeb (Bkemv)

**May 2024 – FDA approved the first interchangeable biosimilar to Soliris**

**November 2024 – FDA approved a new indication for treatment of generalized myasthenia gravis (gMG) in adults who are anti-acetylcholine receptor (AchR) antibody positive**

**FDA Indication:**

- Treatment of patients with paroxysmal nocturnal hemoglobinuria (PNH) to reduce hemolysis
- Treatment of patients with atypical hemolytic uremic syndrome (aHUS) to inhibit complement-mediated thrombotic microangiopathy
- Treatment of generalized myasthenia gravis (gMG) in adult patients who are AchR antibody positive

**Limitation:**

- Not indicated for the treatment of patients with Shiga toxin E. coli related hemolytic uremic syndrome (STEC-HUS)

**Warnings:**

- BBW: Risk of Serious Meningococcal Infections; only available through Bkemv REMS program
  - Complete meningococcal vaccine ≥ 2 weeks before starting unless risks of delaying therapy outweigh risks of developing serious infection
  - Contraindicated for initiation in patients with unresolved serious *Neisseria meningitidis* infections

**Recommended Dosage:**

- Administered by intravenous infusion only
- Dosing stratified by indication, age, and body weight

**Availability:**

- Injection: 300 mg/30 mL (10 mg/mL) in a single-dose vial

# PNH Agents

## eculizumab-aagh (Epysqli)

**July 2024 – FDA approved a biosimilar to Soliris**

**November 2024 – FDA approved a new indication for treatment of generalized myasthenia gravis (gMG) in adults who are anti-acetylcholine receptor (AchR) antibody positive**

**FDA Indication:**

- **Treatment of patients with PNH to reduce hemolysis**
- **Treatment of patients with aHUS to inhibit complement-mediated thrombotic microangiopathy**
- **Treatment of gMG in adult patients who are AchR antibody positive**

**Limitation:**

- **Not indicated for the treatment of patients with Shiga toxin E. coli related hemolytic uremic syndrome (STEC-HUS)**

**Warnings:**

- **BBW: Risk of Serious Meningococcal Infections; only available through Epysqli REMS program**
  - **Complete meningococcal vaccine ≥ 2 weeks before starting unless risks of delaying therapy outweigh risks of developing serious infection**
  - **Contraindicated for initiation in patients with unresolved serious *Neisseria meningitidis* infections**

**Recommended Dosage:**

- **Administered by intravenous infusion only**
- **Dosing stratified by indication, age, and body weight**

**Availability:**

- **Injection: 300 mg/30 mL (10 mg/mL) in a single-dose vial**

# PNH Agents

## eculizumab (Soliris)

**March 2025 – FDA expanded the indication for treatment of generalized myasthenia gravis (gMG) in patients who are anti-acetylcholine receptor (AChR) antibody positive to include pediatrics ≥ 6 years old**

**FDA Indication:**

- Treatment of patients with paroxysmal nocturnal hemoglobinuria (PNH) to reduce hemolysis
- Treatment of patients with aHUS to inhibit complement-mediated thrombotic microangiopathy
- **Treatment of gMG in adult and pediatric patients ≥ 6 years of age who are AChR antibody positive**
- Treatment of neuromyelitis optica spectrum disorder (NMOSD) in adult patients who are anti-aquaporin-4 (AQP4) antibody positive

**Limitation:**

- Not indicated for the treatment of patients with Shiga toxin E. coli related hemolytic uremic syndrome (STEC-HUS)

**Warnings:**

- BBW: Risk of Serious Meningococcal Infections; only available through Epysqli REMS program
  - Complete meningococcal vaccine ≥ 2 weeks before starting unless risks of delaying therapy outweigh risks of developing serious infection
  - Contraindicated for initiation in patients with unresolved serious *Neisseria meningitidis* infections

**Recommended Dosage:**

- **Administered by intravenous infusion only**
- **Dosing stratified by indication, age, and body weight**

**Availability:**

- Injection: 300 mg/30 mL (10 mg/mL) in a single-dose vial

# Immunomodulators, miscellaneous

## NEUROMUSCULAR AGENTS : ANTIMYASTHENIC/CHOLINERGIC AGENTS

# Disease State Description - Immunomodulators, miscellaneous

## Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)

- Rare neurological autoimmune disorder, in which the body attacks the myelin sheaths
- Develops during any decade of life with an average age onset of 50
- Affects males twice as often as females
- Prevalence of ~5-7 cases per 100,000 individuals
- Symptoms include tingling, gradual weakness, or loss of feelings of the arms and legs, and loss of reflexes, balance, or ability to walk
- The best studied treatments that have been shown to be effective are glucocorticoids (steroids), intravenous immunoglobulin (IVIG) and plasma exchange

# Immunomodulators, miscellaneous

## efgartigimod alfa / hyaluronidase-qvfc (Vyvgart Hytrulo)

**June 2024 – FDA approved a new indication for treatment of chronic inflammatory demyelinating polyneuropathy (CIDP) in adults**

**April 2025 – FDA approved a single-dose prefilled syringe formulation containing 1,000 mg of efgartigimod alfa and 10,000 units of hyaluronidase per 5 mL (200 mg/2,000 units per mL)**

**FDA Indication:**

- Treatment of generalized myasthenia gravis (gMG) in adult patients who are AchR antibody positive
- **Treatment of chronic inflammatory demyelinating polyneuropathy (CIDP) in adult patients**

**Warnings:**

- Infections, infusion/injection-related reactions, and hypersensitivity reactions including anaphylaxis, hypotension leading to syncope, angioedema, dyspnea, rash, and urticaria

**Recommended Dosage:**

- **Prefilled syringe can be administered by patients and/or caregivers**
  - **1,000 mg/10,000 units subcutaneously into the abdomen over 20 to 30 seconds in cycles of once weekly injections** (4 weeks for gMG)
- **Vial to be administered with a winged infusion set by a healthcare professional only**
  - **1,008 mg / 11,200 units subcutaneously over 30 to 90 seconds in cycles of once weekly injections** (4 weeks for gMG)

**Availability:**

- **Single-dose prefilled syringe: 1,000 mg efgartigimod alfa and 10,000 units hyaluronidase per 5 mL (200 mg/2,000 units per mL)**
- Single-dose vial: 1,008 mg efgartigimod alfa and 11,200 units hyaluronidase per 5.6 mL (180 mg/2,000 units per mL)

# Oncology - Breast

## ONCOLOGY AGENTS : ANTINEOPLASTICS COMBINATIONS – ORAL
## ONCOLOGY AGENTS : CYCLIN DEPENDENT KINASES (CDK) INHIBITORS – ORAL

# Disease State Description - Oncology - Breast

## Breast Cancer

- Second most common cancer site for women in the United States (US), accounting for 30% of all new cancer diagnoses
- Breast cancer incidence in U.S. women is increasing by approximately 0.5% per year and remains the second leading cause of cancer death after lung cancer
- Death rates from breast cancer have declined by 43% since 1989, largely due to improvements in both early detection and treatment
  - 5-year survival rates in women diagnosed with breast cancer:
    - Overall: 91%
    - Localized disease: > 99%
    - Distant metastatic disease: 32%
- Breast cancer is typically diagnosed in women between the ages of 55 to 74 with the median age of 63 years
- Breast cancer is rarely diagnosed in men

# Guidelines - Oncology - Breast

## National Comprehensive Cancer Network (NCCN) – Breast Cancer, 2025

- **Systemic Adjuvant Therapy**
  - Ribociclib added as a recommended option adjuvant therapy for premenopausal, chemo-ineligible patients with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative breast cancer
  - Abemaciclib remains a preferred adjuvant therapy for high-risk, node-positive HR-positive (HR+), HER2-negative (HER2-) patients after chemotherapy
  - Olaparib added as an option for HR+/HER2- patients with germline BRCA 1/2 mutations who have completed chemotherapy and are considered high-risk
    - Previously recommended only for patients with adjuvant treatment of triple-negative breast cancer (TNBC) with germline BRCA mutation
- **Metastatic Breast Cancer**
  - Abemaciclib + fulvestrant + trastuzumab added for patients with HR+/HER+ disease (Category 2B)
  - For HER2-low disease:
    - Fam-trastuzumab deruxtecan-nxki was downgraded from a preferred (Category 1) to a Category 2A recommendation
    - Datopotamab deruxtecan was added as an option for second-line treatment

# Oncology - Breast

## ribociclib (Kisqali)

**July 2024 – FDA approved expanded indication for treatment of hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer in combination with fulvestrant as initial endocrine-based therapy or following disease progression on endocrine therapy to include all patients**

**September 2024 – FDA approved in combination with an aromatase inhibitor for the adjuvant treatment of adults with HR-positive, HER2-negative stage II and III early breast cancer at high risk of recurrence**

### FDA Indication:

- **In combination with an aromatase inhibitor for the adjuvant treatment of adults with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative stage II and III early breast cancer at high risk of recurrence**
- **Treatment of adults with HR-positive, HER2-negative advanced or metastatic breast cancer in combination with:**
  - An aromatase inhibitor as initial endocrine-based therapy; or
  - **Fulvestrant as initial endocrine-based therapy or following disease progression on endocrine therapy**

### Warnings:

- Interstitial lung disease (ILD)/pneumonitis, QT prolongation, increased QT prolongation with concomitant use of tamoxifen, hepatotoxicity, neutropenia, embryo-fetal toxicity, and severe cutaneous adverse reactions (SCARs)

### Recommended Dosage:

- **Early Breast Cancer Starting Dose: 400 mg orally once daily for 21 consecutive days followed by 7 days off treatment**
- **Advanced or Metastatic Breast Cancer Starting Dose: 600 mg orally once daily for 21 consecutive days followed by 7 days off treatment**
- **Dose interruption, reduction, and/or discontinuation may be required based on individual safety and tolerability**

### Availability:

- Tablets: 200 mg

# Oncology - Breast

## palbociclib (Ibrance)

**April 2025 – FDA approved new indication for in combination with inavolisib and fulvestrant for the treatment of adult patients with endocrine-resistant, PIK3CA-mutated, hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative, locally advanced or metastatic breast cancer, as detected by an FDA-approved test, following recurrence on or after completing adjuvant endocrine therapy**

**FDA Indication:**

- Treatment of adult patients with HR-positive, HER2-negative advanced or metastatic breast cancer in combination with:
  - an aromatase inhibitor as initial endocrine-based therapy; or
  - fulvestrant in patients with disease progression following endocrine therapy
- **In combination with inavolisib and fulvestrant for the treatment of adult patients with endocrine-resistant, PIK3CA-mutated, HR-positive, HER2-negative, locally advanced or metastatic breast cancer, as detected by an FDA-approved test, following recurrence on or after completing adjuvant endocrine therapy**

**Warnings:**

- Neutropenia, interstitial lung disease (ILD)/pneumonitis, embryo-fetal toxicity

**Recommended Dosage:**

- **Starting Dose: 125 mg once daily taken with food for 21 days followed by 7 days off treatment**
- **Interrupt or reduce dose based on individual safety and tolerability**

**Availability:**

- Capsules: 125 mg, 100 mg, and 75 mg
- **Tablets: 125 mg, 100 mg, and 75 mg**

# Oncology - Skin and Other

## ONCOLOGY AGENTS : BRAF KINASE INHIBITORS – ORAL
## ONCOLOGY AGENTS : MEK INHIBITORS - ORAL

# Disease State Description - Oncology - Skin and Other

## Pediatric Lowgrade Glioma (LGG)

- Group of slow-growing tumors that occurs throughout the brain and spinal cord and the most common of the pediatric central nervous system (CNS) cancers
- Rarely spread beyond the site of origin and are often benign
- Symptoms are dependent on the location of the tumor but may include vision changes, headache, vomiting, or balance issues

## National Comprehensive Cancer Network (NCCN) – Pediatric Central Nervous System Cancers, 2025

- Excellent prognosis: Cure is often possible when surgical resection is feasible (~80% diagnosed with LGG)
- Some patients may not be surgical candidates due to the location of the tumor and other patients may demonstrate more aggressive tumor biology, necessitating other treatment measures
  - Chemotherapy: Vincristine plus carboplatin and/or radiotherapy may be used in this setting
  - Targeted Therapies: BRAF inhibitors and MEK inhibitors

# Oncology - Skin and Other

## tovorafenib (Ojemda)

**April 2024 – FDA granted new drug under accelerated approval based on response rate and duration of response for the treatment of patients ≥ 6 months of age with relapsed or refractory pediatric lowgrade glioma (LGG) harboring a BRAF fusion or rearrangement, or BRAF V600 mutation**

- **Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s)**

**Warnings:**

- **Hemorrhage, skin toxicity including photosensitivity, hepatotoxicity, reductions in growth velocity, embryo-fetal toxicity, and neurofibromatosis type 1 (NF1) associated tumors**

**Recommended Dosage:**

- **Based on body surface area (BSA): 380 mg/m$^2$ orally once weekly (maximum 600 mg once weekly) until disease progression or intolerable toxicity**
- **Recommended dosage for patients with body surface area (BSA) < 0.3 m$^2$ has not been established**

**Availability:**

- **Tablets: 100 mg**
- **Oral Suspension: 25 mg/mL**

# Disease State Description - Oncology - Skin and Other

## Plexiform Neurofibromas (PN)

- Plexiform neurofibromas (PN) are peripheral nerve sheath tumors that cause significant disfigurement, morbidity, and mortality in patients with NF1
- Neurofibromatosis type 1 (NF1) is an autosomal dominant genetic disorder leading to overactivation of signaling pathways and subsequent tumor formation
- Benign and malignant tumors form in patients with NF1, the most common of which are neurofibromas
- Surgery resection is an option but is limited due to infiltration patterns and growth along the spinal column
- MEK inhibitors:
  - Selumetinib was the first FDA approved therapy for patients with NF1 and symptomatic PN
    - Indicated for pediatric patients 2 years of age and older with NF1 and inoperable PN
  - Mirdametinib is the second MEK inhibitor approved for systemic PN associated with inoperable NF1

# Oncology - Skin and Other

## mirdametinib (Gomekli)

**July 2024 – FDA approved new drug for the treatment of adults and pediatric patients ≥ 2 years of age with neurofibromatosis type 1 (NF1) who have symptomatic plexiform neurofibromas (PN) not amenable to complete resection**

**Warnings:**

- **Ocular toxicity: Eye exams before and regularly during treatment; If vision changes occurs, adjust dose or discontinue based on severity**
- **Left ventricular dysfunction: Echocardiogram before, every 3 months during first year, then as needed during treatment; adjust dose or discontinue based on cardiac function**
- **Dermatologic adverse reactions: Start supportive care at first sign; Adjust or discontinue treatment based on severity**
- **Embryo-fetal toxicity: May cause fetal harm; Counsel on effective contraception use**

**Recommended Dosage:**

- **Based on body surface area (BSA): 2 mg/m$^2$ orally twice daily, with or without food, for the first 21 days of each 28-day cycle until disease progression or unacceptable toxicity**

**Availability:**

- **Capsules: 1 mg and 2 mg**
- **Tablets for Oral Suspension: 1 mg**

# Disease State Description - Oncology - Skin and Other

## 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) – Colon Cancer, 2025

- Metastatic Colorectal Cancer (mCRC) with BRAF V600E mutation
  - Initial Treatment: Encorafenib + EGFR inhibitor (cetuximab or panitumumab) + FOLFOX chemotherapy for patients eligible for intensive therapy (Category 2A)
  - Second-line and Subsequent Therapy (if not previously given): Encorafenib + EGFR inhibitor (cetuximab or panitumumab) (Category 2B)

# Oncology - Skin and Other

## encorafenib (Braftovi)

**December 2024 – FDA granted new indication under accelerated approval based on response rate and duration of response for in combination with cetuximab and mFOLFOX6, for the treatment of patients with metastatic colorectal cancer (mCRC) with a BRAF V600E mutation, as detected by an FDA-approved test**

- **Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s)**

### FDA Indication:

- In combination with binimetinib, for the treatment of patients with unresectable or metastatic melanoma with a BRAF V600E or V600K mutation, as detected by an FDA-approved test
- **In combination with cetuximab and mFOLFOX6, for the treatment of patients with metastatic colorectal cancer (mCRC) with a BRAF V600E mutation, as detected by an FDA-approved test under accelerated approval**
- In combination with cetuximab, for the treatment of adult patients with metastatic CRC with a BRAF V600E mutation, as detected by an FDA-approved test, after prior therapy
- In combination with binimetinib, for the treatment of adult patients with metastatic non-small cell lung cancer (NSCLC) with a BRAF V600E mutation, as detected by an FDA-approved test

### Warnings:

- New primary malignancies (cutaneous and noncutaneous), tumor promotion in BRAF wild-type tumors, cardiomyopathy, hepatoxicity, hemorrhage, uveitis, QT prolongation, embryo-fetal toxicity

### Recommended Dosage:

- Melanoma: 450 mg orally once daily
- **CRC: 300 mg orally once daily**
- NSCLC: 450 mg orally once daily

### Availability:

- Capsules: 75 mg

# Disease State Description - Oncology - Skin and Other

## Ovarian Cancer

- One of the leading causes of cancer deaths among women
- Lifetime risk for a women: 1 in 91
- Primarily affects older women: Half of cases are diagnosed at age 63 years and older
- The incidence rate has been declining and is likely due to increased use of oral contraceptives and reduced menopausal hormone therapy
- Mortality rate has also decreased due to better treatments and fewer diagnosis

## National Comprehensive Cancer Network (NCCN) – Ovarian Cancer, 2025

- Low-Grade Serous Ovarian Cancer (LGSOC)
  - First Line: Surgery with goal of optimal cytoreduction
    - Adjuvant Therapy: Hormonal therapy or chemotherapy
  - Maintenance: Hormone therapy
  - Recurrent LGSOC:
    - Hormone therapy
    - Chemotherapy (if not previously used)
    - Systemic therapy:
      - KRAS mutation: avutometinib + defactinib is recommended (Category 2A)
      - Trametinib (Category 2A)
      - Binimetinib (Category 2B)

# Oncology - Skin and Other

## (avutometinib and defactinib) Avmapki Fakzynja Co-Pack

**May 2025 – FDA approved a combination of avutometinib and defactinib under accelerated approval based on tumor response rate and duration of response, indicated for the treatment of adult patients with KRAS-mutated recurrent low-grade serous ovarian cancer (LGSOC) who have received prior systemic therapy**

**Warnings:**

- **Ocular toxicities: Eye exam at baseline, prior to cycle 2, and every 3 cycles thereafter, and as clinically indicated**
- **Serious skin toxicities: Topical corticosteroid or systemic oral antibiotics with initiation and during therapy for at least the first 2 cycles**
- **Hepatotoxicity: Monitor liver function tests prior to each cycle, on day 15 of the first 4 cycles, and as clinically indicated**
- **Rhabdomyolysis: Monitor creatine phosphokinase prior to each cycle, on day 15 of the first 4 cycles, and as clinically indicated**
- **Embryo-fetal toxicity**
- **Lactation: Advise not to breastfeed**
- **Infertility: May impair fertility in male and females**

**Recommended Dosage:**

- **Avmapki (avutometinib): 3.2 mg orally twice weekly (Day 1 and Day 4) for the first 3 weeks of each 4-week cycle**
- **Fakzynja (dafactinib): 200 mg orally twice daily for the first 3 weeks of each 4-week cycle**
- **Continued until disease progression or unacceptable toxicity**

**Availability:**

- **Avmapki capsules: 0.8 mg**
- **Fakzynja tablets: 200 mg**

# Oncology - Lung

## ONCOLOGY AGENTS : TROPOMYOSIN RECEPTOR KINASE INHIBITORS - ORAL

# Disease State Description – Tropomyosin Receptor Kinase Inhibitors – Oral

## Neurotrophic Tyrosine Receptor Kinase (NTRK)

- Neurotrophic receptor tyrosine kinase (NTRK) gene fusions have been identified in a number of adult and pediatric cancers
- Distribution follows two general patterns
  - Rare cancers enriched with NTRK fusions (e.g. secretory breast carcinoma and mammary analog secretory carcinoma [MASC] of the salivary gland)
  - Common cancers with rare NTRK fusions (e.g. colon cancer, bladder cancer, and non-small cell lung cancer [NSCLC])

### The Japan Society of Clinical Oncology/European Society of Medical Oncology/American Society of Clinical Oncology/ Japanese Society of Medical Oncology/Taiwan Oncology Society (JSCO/ESMO/ASCO/JSMO/TOS) international expert consensus recommendations for tumor-agnostic treatments in patients with solid tumors with microsatellite instability or NTRK fusions, 2020

- Patients with advanced unresectable or metastatic solid tumors without actionable driver gene mutations/amplifications/fusions should be tested for NTRK fusion status
- Patients with advanced unresectable or metastatic solid tumors that are highly likely to harbor NTRK fusions should be tested
- Patients with locally advanced tumors with a high incidence of NTRK fusions should be tested when considering neoadjuvant therapy prior to surgical resection
- The tropomyosin receptor kinase (TRK) inhibitors are strongly recommended for patients positive for NTRK fusions, particularly when no other satisfactory treatment options are available, depending upon the clinical context

# Oncology - Tropomyosin Receptor Kinase Inhibitors – Oral

## repotrectinib (Augtyro)

**June 2024 – FDA granted accelerated approval based on overall response rate and duration of response for treatment of adults and pediatric patients ≥ 12 years of age with solid tumors that: (1) have a neurotrophic tyrosine receptor kinase (NTRK) gene fusion, (2) are locally advanced or metastatic or where surgical resection is likely to result in severe morbidity, and (3) have progressed following treatment or have no satisfactory alternative therapy**

- **Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s)**

**FDA Indication:**

- Treatment of adult patients with locally advanced or metastatic *ROS1*-positive nonsmall cell lung cancer (NSCLC)
- **Treatment of adult and pediatric patients ≥ 12 years of age under accelerated approval with solid tumors that:**
  - **Have a neurotrophic tyrosine receptor kinase (NTRK) gene fusion and**
  - **Are locally advanced or metastatic or where surgical resection is likely to result in severe morbidity**
  - **Have progressed following treatment or have no satisfactory alternative therapy**

**Warnings:**

- Interstitial lung disease (ILD)/pneumonitis, hepatotoxicity, embryo-fetal toxicity, myalgia with creatine phosphokinase (CPK) elevation, hyperuricemia, skeletal fractures, and central nervous system (CNS) effects including dizziness, ataxia, and cognitive impairment

**Recommended Dosage:**

- **160 mg orally once daily for 14 days, then increase to 160 mg twice daily until disease progression or unacceptable toxicity**

**Availability:**

- Capsules: 40 mg, 160 mg

# Oncology – Breast, Hematologic, Lung, Renal, Other

## ONCOLOGY AGENTS : TYROSINE KINASE INHIBITORS - ORAL

# Disease State Description – Oncology - Tyrosine Kinase Inhibitors – Oral

## Lung Cancer

- Leading cause of cancer death in both men and women in the United States (US) with a 5-year survival ~28.1%
  - Declines in lung cancer diagnosis and mortality in the US in the recent years
  - Despite these encouraging trends, there are still more US lung cancer deaths annually than deaths from breast cancer and prostate cancer combined
- The primary risk factor for the development of lung cancer is smoking tobacco, accounting for approximately 85% to 90% of all cases of lung cancer
- The USPSTF guidelines recommends annual lung cancer screening with  low-dose computed tomography (CT) for patients 50 to 80 years old who are current smokers with at least a 20 pack-year smoking history and former smokers who have quit within the past 15 years

# Guidelines - Oncology - Tyrosine Kinase Inhibitors – Oral

## NCCN Guidelines – Non-Small Cell Lung Cancer (NSCL), 2025

- **ALK-rearranged NSCL cancer discovered before first-line systemic therapy:**
  - Ensartinib added as preferred first-line and subsequent therapy
  - Ceritinib moved from other recommended to useful in certain circumstances for first-line therapy
- **ALK-rearranged NSCL cancer discovered during first-line systemic therapy:**
  - First line therapy: Interrupt current therapy and start, followed by Alectinib (preferred) or Brigatinib (preferred) or Ensartinib (preferred) or Lorlatinib (preferred) or Ceritinib or Crizotinib
  - Ensartinib added as preferred first-line and subsequent therapy
- **EGFR Exon 19 Deletions or Exon 21 L858R mutations discovered during first-line systemic therapy:**
  - Add osimertinib to pemetrexed + (cisplantin or carboplantin) (nonsquamous) or
  - Interrupt current therapy and start osimertinib or amivantamab-vmjw + lazertinib or
  - Afatinib or dacomitinib or erlotinib or erlotinib + bevacizumab or erlotinib + ramuciramab or gefitinib
- **EGFR S768I, L861Q, and/or G719X mutations discovered during first-line systemic therapy:**
  - Interrupt current therapy and start afatinib (preferred) or osimertinib (preferred) or dacomitinib or erlotinib or gefitinib

# Disease State Description - Oncology - Tyrosine Kinase Inhibitors – Oral

## Thyroid Cancer

- Three main types:
  - **Differentiated thyroid carcinoma (DTC):** Most Common, 85% to 95% of thyroid cancer cases
    - Includes follicular, papillary, and oncocytic carcinomas
  - **Medullary thyroid carcinoma (MTC):** Neuroendocrine tumors that do not concentrate iodine and do not respond well to conventional chemotherapy
  - **Anaplastic thyroid carcinoma (ATC):** Rare, extremely aggressive with a mortality rate approaching 100%
- DTC and MTC: Surgery is the initial treatment modality
- ATC: Surgery is only utilized when complete resection is a possibility as surgical debulking has not been shown to improve patient outcomes or survival for this population
- Systemic therapies are recommended for patients with surgically unresectable disease in DTC and MTC and can also be offered to patients with ATC

# Guidelines - Oncology - Tyrosine Kinase Inhibitors – Oral

## NCCN Guidelines – Thyroid Carcinoma 2025

- Recommends somatic testing to identify actionable mutations (ALK rearrangements, NTRK gene fusions, BRAF V600E mutation, and RET gene fusions) and markers (tumor mutational burden, microsatellite instability, and mismatch repair deficiency)
- New systemic treatment options are tailored to specific mutations:
  - RET fusion-positive or RET- mutant tumors: Selpercatinib and pralsetinib
  - BRAF V600E mutation positive: Dabrafenib + trametinib
  - NTRK gene fusion-positive tumors: Larotrectinib, entrectinib, repotrectinib
- Radioactive iodine therapy is no longer routinely recommended for all postoperative patients with differentiated thyroid cancer Use is more selective – guided by tumor size, histology, lymph node involvement, thyroglobulin (Tg) levels, and other clinicopathologic features
- Kinase inhibitor therapy should be reserved for patients with progressive or symptomatic disease, rather than those with very indolent disease who are asymptomatic

## Chronic Myeloid Leukemia (CML)

- Defined by the presence of the Philadelphia chromosome (Ph) in a patient with a myeloproliferative neoplasm (MPN)
  - The Philadelphia chromosome is a result of a chromosomal translocation between chromosomes 9 and 22 [t(9:22)] which gives rise to the BCR-ABL fusion gene
  - Deregulated activity and plays a central role in the pathogenesis of CML
- CML occurs in 3 phases: chronic phase (CP), accelerated phase (AP), and blast phase (BP)
  - Approximately 90-95% of cases are diagnosed in CP
  - If CP-CML is left untreated: Progress to advanced phase CML (AP-/BP-CML) within 3-5 years

## NCCN Guidelines – Chronic Myeloid Leukemia, 2025

- First-line therapy in chronic-phase CML across all risk scores:
  - First generation tyrosine kinase inhibitor (TKI): imatinib
  - Second generation TKI: bosutinib, dasatinib, nilotinib
  - Allosteric TKI: asciminib
  - Clinical trial
- Asciminib added as a treatment option for patients with CP-CML with T315I mutation and/or previously treated CP-CML

# Disease State Description - Oncology - Tyrosine Kinase Inhibitors – Oral

## Mantle Cell Lymphoma (MCL)

- MCL, while technically classified as an aggressive lymphoma, possesses characteristics of both indolent and aggressive NHLs
- The median overall survival is approximately 4 to 5 years, but there is no evidence of a survival plateau, which is similar to indolent lymphomas
- The chromosomal translocation t(11;14) is usually present in MCL
- MCL is highly resistant to conventional chemotherapy and displays an aggressive disease course

## National Comprehensive Cancer Network (NCCN), 2025 – B-Cell Lymphomas

- Mantel Cell Lymphoma Guidelines
  - Less aggressive induction therapy, preferred regimens:
    - Acalabrutinib (continuous) + bendamustine + rituximab
    - Bendamustine + rituximab
    - VR-CAP (bortezomib, rituximab, cyclophosphamide, doxorubicin, and prednisone)
    - RCHOP
    - Lenalidomide (continuous) + rituximab
  - Less aggressive induction therapy, other recommended regimen
    - Acalabrutinib (continuous) + rituximab

# Disease State Description - Oncology - Tyrosine Kinase Inhibitors – Oral

## Tenosynovial Giant Cell Tumor (TGCT)

- Rare, benign, and typically non-life-threatening tumors that occurs in the synovium, bursae, and tendon sheath (parts of the joint or tendon lining)
- Localized TGCT: Usually smaller joints affected (fingers or toes)
  - Slow-growing and well-defined (encapsulated)
  - Often curable with surgical removal
- Diffuse TGCT (also known as diffuse-type giant cell tumor): Usually affects large joints (most common: knees)
  - Previously known as pigmented villonodular synovitis (PVNS)
  - Progressive and can progress to arthritic damage and degeneration to the joint and damage the surrounding cartilage and bone
  - Surgery is the mainstay of treatment; however, disease often recurs

## National Comprehensive Cancer Network (NCCN), 2025 – Soft Tissue Sarcoma

- Tenosynovial Giant Cell Tumor/Pigmented Villonodular Synovitis
  - Preferred Regimens: pexidartinib or vimseltinib (category 1)
  - Useful in certain circumstances: imatinib or nilotinib

# Disease State Description - Oncology - Tyrosine Kinase Inhibitors – Oral

## Neuroendocrine Tumors (NETs)

- Pancreatic neuroendocrine tumors (pNETs) are islet cell tumors that forms in the hormone-producing cells of the pancreas
  - Less common type (< 2%)  of pancreatic cancers
  - Better prognosis compared to common type of pancreatic cancers
- Extra-pancreatic NETs (epNETs) are neuroendocrine tumor that arises outside of the pancreas (e.g. small intestine, lungs, rectum)
- Treatment depends on tumor grade, functional status, and extent of disease
  - Resectable Tumors: Surgery is recommended and is usually all that is needed for many NETs
  - Unresectable Tumors:
    - Observation considered in select indolent, non-functional, and asymptomatic tumors
    - Somatostatin analogs useful in somatostatin receptor-positive NETs or carcinoid syndrome (e.g. diarrhea, facial flushing, wheezing, rapid heart rate)
    - For advance, metastatic, or progressive despite initial treatments, chemotherapy or targeted drugs (e.g. cabozantinib, everolimus) can be used
    - Radiation treatment is also an option for adults with pNETs that are somatostatin receptor-positive

# Oncology - Tyrosine Kinase Inhibitors – Oral

## alectinib (Alecensa)

**April 2024 – FDA approved a new indication for adjuvant treatment in adult patients following tumor resection of anaplastic lymphoma kinase (ALK)-positive non-small cell lung cancer (NSCLC) (tumors ≥ 4 cm or node positive) as detected by an FDA-approved test**

**FDA Indication:**

- **Adjuvant treatment in adult patients following tumor resection of ALK-positive NSCLC (tumors ≥ 4 cm or node positive) as detected by an FDA-approved test**
- Treatment of adult patients with ALK-positive metastatic NSCLC as detected by an FDA-approved test

**Warnings:**

- Interstitial lung disease (ILD)/pneumonitis, hepatotoxicity, embryo-fetal toxicity, renal impairment, bradycardia, hemolytic anemia, and severe myalgia and creatine phosphokinase (CPK) elevation

**Recommended Dosage:**

- **Starting dose: 600 mg orally twice daily with food until disease recurrence or unacceptable toxicity (or a total of 2 years for adjuvant treatment of resected NSCLC)**
- **Severe hepatic impairment: 450 mg twice daily**

**Availability:**

- Capsules: 150 mg

# Oncology - Tyrosine Kinase Inhibitors – Oral

## selpercatinib (Retevmo)

**May 2024 – FDA granted accelerated approval for pediatric patients ≥ 2 years for: (1) advanced or metastatic medullary thyroid cancer (MTC) with a RET mutation, (2) advanced or metastatic thyroid cancer with a RET gene fusion, who require systemic treatment and are radioactive iodine-refractory (if radioactive iodine is appropriate), and (3) locally advanced or metastatic solid tumors with a RET gene fusion, that have progressed on or following prior systemic therapy or who have no satisfactory alternative treatment options**

**June 2024 – FDA granted traditional approval for advanced or metastatic thyroid cancer with a RET gene fusion indication**

**October 2024 – FDA granted traditional approval for advanced or metastatic MTC with a RET mutation indication**

**FDA Indication:**

- Adult patients with locally advanced or metastatic NSCLC with a rearranged during transfection (RET) gene fusion, as detected by an FDA-approved test
- **Adult and pediatric patients ≥ 2 years of age with:**
  - **Advanced or metastatic MTC with a RET mutation, as detected by an FDA-approved test, who require systemic therapy**
  - **Advanced or metastatic thyroid cancer with a RET gene fusion, as detected by an FDA-approved test, who require systemic therapy and who are radioactive iodine-refractory (if radioactive iodine is appropriate)**
  - **Locally advanced or metastatic solid tumors with a RET gene fusion, as detected by an FDA-approved test, that have progressed on or following prior systemic treatment or who have no satisfactory alternative treatment options under accelerated approval**
    - **Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s)**

# Oncology - Tyrosine Kinase Inhibitors – Oral

## selpercatinib (Retevmo)

**Warnings:**

- Interstitial lung disease (ILD)/pneumonitis, hepatotoxicity, embryo-fetal toxicity, hypertension, QT interval prolongation, hemorrhagic events, hypersensitivity, tumor lysis syndrome, risk of impaired wound healing, hypothyroidism, and slipped capital femoral epiphysis/slipped upper femoral epiphysis (SCFE/SUFE) in pediatric patients

**Recommended Dosage:**

- **Patients 2 to <12 years of age based on body surface area (BSA)**
  - **<0.33 $m^2$: Not recommended**
  - **0.33 to 0.65 $m^2$: 40 mg orally three times daily**
  - **0.66 to 1.08 $m^2$: 80 mg orally twice daily**
  - **1.09 to 1.52 $m^2$: 120 mg orally twice daily**
  - **≥ 1.53 $m^2$: 160 mg orally twice daily**
- **Patients ≥ 12 years old based on body weight**
  - **< 50 kg: 120 mg orally twice daily**
  - **≥ 50 kg: 160 mg orally twice daily**
- **Continue treatment until disease progression or unacceptable toxicity**
- **Severe hepatic impairment: Reduce dose**

**Availability:**

- Capsules: 40 mg, 80 mg
- Tablets: 40 mg, 80 mg, 120 mg, 160 mg

# Oncology - Tyrosine Kinase Inhibitors – Oral

## lazertinib (Lazcluze)

**August 2024 – FDA approved new drug for use in combination with amivantamab for first-line treatment of adults with locally advanced or metastatic NSCLC with EGFR exon 19 deletions or exon 21 L858R substitution mutations, as detected by an FDA-approved test.**

**Warnings:**

- **Venous Thromboembolic Events (VTE): Prophylactic anticoagulation is recommended for the first four months of treatment; Monitor for signs and symptoms of VTE and treat as medically appropriate**
- **Interstitial Lung Disease (ILD)/pneumonitis, severe rash including acneiform dermatitis, new or worsening signs and symptoms of ocular adverse reactions including keratitis, and embryo-fetal toxicity**

**Recommended Dosage:**

- **240 mg orally once daily in combination with amivantamab**

**Availability:**

- **Tablets: 80 mg and 240 mg**

# Oncology - Tyrosine Kinase Inhibitors – Oral

## osimertinib (Tagrisso)

**September 2024 – FDA approved new indication for treatment of adult patients with locally advanced, unresectable (stage III) NSCLC whose disease has not progressed during or following concurrent or sequential platinum-based chemoradiation therapy and whose tumors have EGFR exon 19 deletions or exon 21 L858R mutations, as detected by an FDA-approved test**

**FDA Indication:**

- Adjuvant therapy after tumor resection in adult patients with NSCLC whose tumors have epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 L858R mutations, as detected by an FDA-approved test
- **Treatment of adult patients with locally advanced, unresectable (stage III) NSCLC whose disease has not progressed during or following concurrent or sequential platinum-based chemoradiation therapy and whose tumors have EGFR exon 19 deletions or exon 21 L858R mutations, as detected by an FDA-approved test**
- First-line treatment of adult patients with metastatic NSCLC whose tumors have EGFR exon 19 deletions or exon 21 L858R mutations, as detected by an FDA-approved test
- In combination with pemetrexed and platinum-based chemotherapy, the first-line treatment of adult patients with locally advanced or metastatic NSCLC whose tumors have EGFR exon 19 deletions or exon 21 L858R mutations, as detected by an FDA-approved test
- Treatment of adult patients with metastatic EGFR T790M mutation positive NSCLC, as detected by an FDA-approved test, whose disease has progressed on or after EGFR TKI therapy

# Oncology - Tyrosine Kinase Inhibitors – Oral

## osimertinib (Tagrisso)

**Warnings:**

- Interstitial lung disease (ILD)/pneumonitis, embryo-fetal toxicity, QT interval prolongation, cardiomyopathy, keratitis, erythema multiforme major, Stevens-Johnson syndrome, toxic epidermal necrolysis, cutaneous vasculitis, and aplastic anemia

**Recommended Dosage:**

- Adjuvant treatment of early-stage NSCLC: 80 mg orally once daily until disease recurrence or unacceptable toxicity, or up to 3 years
- **Locally advanced, unresectable (stage III) NSCLC following platinum-based chemoradiation therapy: 80 mg orally once daily until disease progression or unacceptable toxicity**
- Metastatic NSCLC: 80 mg orally once daily until disease progression or unacceptable toxicity
- Locally advanced or metastatic NSCLC: 80 mg orally once daily with pemetrexed and platinum-based chemotherapy until disease progression or unacceptable toxicity

**Availability:**

- Tablets: 80 mg and 40 mg

# Oncology - Tyrosine Kinase Inhibitors – Oral

## inavolisib (Itovebi)

**October 2024 – FDA approved a new drug for use in combination with palbociclib and fulvestrant for treatment of adults with endocrine-resistant, *PIK3CA*-mutated, HR-positive, HER2-negative, locally advanced or metastatic breast cancer, as detected by an FDA-approved test, following recurrence on or after completing adjuvant endocrine therapy**

**Warnings:**

- **Hyperglycemia, stomatitis, diarrhea, embryo-fetal toxicity**

**Recommended Dosage:**

- **9 mg orally once daily until disease progression or unacceptable toxicity**
- **Moderate renal impairment: Reduce starting dose**

**Availability:**

- **Tablets: 3 mg and 9 mg**

# Oncology - Tyrosine Kinase Inhibitors – Oral

## Manufacture Communication

- **November 2024 - pralsetinib (Gavreto)**
  - Rigel issued a safety alert for increased risk of severe and fatal infection, including severe opportunistic infection
  - Prescribers are advised to monitor for signs and symptoms of infection and to treat based on local and institutional guidelines

# Oncology - Tyrosine Kinase Inhibitors – Oral

## asciminib (Scemblix)

**November 2024 – FDA granted new indication under accelerated approval based on major molecular response rate for treatment of adults with newly diagnosed Philadelphia chromosome-positive (Ph+) CML in chronic phase (CP)**

- **Continued approval for this indication may be contingent upon verification of clinical benefit in a confirmatory trial(s)**

**November 2024 - Indication for previously treated Ph+ CML in CP has been revised**

- **Previously, patients with Ph+ CML in CP had to receive treatment with ≥ 2 tyrosine kinase inhibitors before Scemblix could be prescribed**

### FDA Indication:

- **Treatment of newly diagnosed Ph+ CML in CP in adult patients under accelerated approval**
- **Treatment of previously treated Ph+ CML in CP in adult patients**
- Treatment of Ph+ CML in CP with the T315I mutation in adult patients

### Warnings:

- Myelosuppression, pancreatic toxicity, hypertension, hypersensitivity, cardiovascular toxicity, and embryo-fetal toxicity

### Recommended Dosage:

- **Ph+ CML in CP: 80 mg orally once daily or 40 mg orally twice daily**
- **Ph+ CML in CP with the T315I Mutation: 200 mg orally twice daily**
- **Avoid food for at least 2 hours before and 1 hour after dose**

### Availability:

- Film-coated tablets: 20 mg, 40 mg, and 100 mg

# Oncology - Tyrosine Kinase Inhibitors – Oral

## nilotinib (Danziten)

**November 2024 – FDA approved new formulation of nilotinib as oral tablets**

**FDA Indication:**

- Treatment of adult patients with newly diagnosed Philadelphia chromosome-positive (Ph+ CML) in chronic phase (CP)
- Treatment of adult patients with chronic phase (CP) and accelerated phase (AP) Ph+ CML resistant to or intolerant to prior therapy that included imatinib

**Warnings:**

- BBW: QT prolongation and sudden deaths
  - Monitor QTc at baseline, seven days after initiation, periodically thereafter, and following any dose adjustments
- CI: hypokalemia, hypomagnesemia, or long QT syndrome
- Myelosuppression, cardiac and arterial vascular occlusive events, pancreatitis, hepatotoxicity, tumor lysis syndrome, hemorrhage, fluid retention, growth and development delay in pediatric patients, and embryo-fetal toxicity
- Not substitutable with other nilotinib products, including other nilotinib tablets, on a milligram per milligram basis

**Recommended Dosage:**

- Newly diagnosed Ph+ CML-CP: 142 mg orally twice daily
- Resistant or intolerant Ph+ CML-CP and CML-AP: 190 mg orally twice daily

**Availability:**

- Tablets: 71 mg and 95 mg

# Oncology - Tyrosine Kinase Inhibitors – Oral

## imatinib (Imkeldi)

**November 2024 – FDA approved a new formulation of imatinib as an oral solution**

**FDA Indication:**

- **Treatment of newly diagnosed adult and pediatric patients with Ph+ CML in chronic phase (CP)**
- **Treatment of patients with Ph+ CML in blast crisis (BC), accelerated phase (AP), or in CP after failure of interferon-alpha therapy**
- **Treatment of adult patients with relapsed or refractory Philadelphia chromosome positive acute lymphoblastic leukemia (Ph+ ALL)**
- **Treatment of pediatric patients with newly diagnosed Ph+ ALL in combination with chemotherapy**
- **Treatment of adult patients with relapsed or refractory Ph+ ALL**
- **Treatment of pediatric patients with newly diagnosed Ph+ ALL in combination with chemotherapy**
- **Treatment of adult patients with myelodysplastic/myeloproliferative diseases (MDS/MPD) associated with platelet-derived growth factor receptor (PDGFR) gene re-arrangements**
- **Treatment of adults with aggressive systemic mastocytosis (ASM) without D816V c-Kit mutation or c-Kit mutational status unknown**
- **Treatment of adults with hypereosinophilic syndrome (HES) and/or chronic eosinophilic leukemia (CEL) who have the FIP1L1-PDGFRα fusion kinase (mutational analysis or fluorescence in situ hybridization [FISH] demonstration of CHIC2 allele deletion) and for patients with HES and/or CEL who are FIP1L1-PDGFRα fusion kinase negative or unknown**
- **Treatment of adult patients with unresectable, recurrent and/or metastatic dermatofibrosarcoma protuberans (DFSP)**
- **Treatment of patients with Kit (CD117) positive unresectable and/or metastatic malignant gastrointestinal stromal tumors (GIST)**
- **Adjuvant treatment of adult patients following resection of Kit (CD117) positive GIST**

# Oncology - Tyrosine Kinase Inhibitors – Oral

## imatinib (Imkeldi)

**Warnings:**

- Fluid retention and edema, hematologic toxicity, congestive heart failure and left ventricular dysfunction, hepatotoxicity, hemorrhage, gastrointestinal disorders, hypereosinophilic cardiac toxicity, dermatologic toxicities, hypothyroidism, embryo-fetal toxicity, growth delay in children and adolescents, tumor lysis syndrome, impairments related to driving and using machinery, renal toxicity

**Recommended Dosage:**

- **Stratified by indication ranging from 100 mg/day to 800 mg/day for adults and 340 mg/m$^2$/day for pediatrics**
- **Taken orally with a meal and large glass of water**
- **400 mg or 600 mg are taken once daily, whereas a dose of 800 mg should be administered as 400 mg twice a day**
- **Dose adjustments are recommended in patients with renal impairment or severe hepatic impairment**

**Availability:**

- **Oral solution: 80 mg/mL**

# Oncology - Tyrosine Kinase Inhibitors – Oral

## acalabrutinib (Calquence)

**January 2025 – FDA approved a new indication for in combination with bendamustine and rituximab for the treatment of adult patients with previously untreated mantle cell lymphoma (MCL) who are ineligible for autologous hematopoietic stem cell transplantation (HSCT)**

**January 2025 – FDA granted traditional approval for MCL in patients who have received ≥ 1 prior therapy**

**FDA Indication:**

- **In combination with bendamustine and rituximab for the treatment of adult patients with previously untreated MCL who are ineligible for autologous HSCT**
- **For the treatment of adult patients with MCL who have received at least one prior therapy**
- For the treatment of adult patients with chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL)

**Warnings:**

- Serious and opportunistic infections, hemorrhage, cytopenia, second primary malignancies, cardiac arrhythmias, hepatotoxicity

**Recommended Dosage:**

- **100 mg orally every 12 hours with water until disease progression or unacceptable toxicity**
- **Severe Hepatic Impairment: Avoid use**

**Availability:**

- Tablets: 100 mg
- Capsules: 100 mg

# Oncology - Tyrosine Kinase Inhibitors – Oral

## vimseltinib (Romvimza)

**February 2025 – FDA approved new drug for treatment of adult patients with symptomatic tenosynovial giant cell tumor (TGCT) for which surgical resection will potentially cause worsening functional limitation or severe morbidity**

**Warnings:**

- **Hepatotoxicity, embryo-fetal toxicity, allergic reactions to FD&C Yellow No. 5 (tartrazine) and No. 6 (Sunset Yellow FCF), and increased serum creatinine without affecting renal function**

**Recommended Dosage:**

- **30 mg orally twice weekly, with a minimum of 72 hours between doses**

**Availability:**

- **Capsules: 14 mg, 20 mg, 30 mg**

# Oncology - Tyrosine Kinase Inhibitors – Oral

## nilotinib D-tartrate

**March 2025 – FDA approved nilotinib D-tartrate capsules for treatment of (1) Adult patients with newly diagnosed Philadelphia chromosome positive chronic myeloid leukemia (Ph+ CML) in chronic phase or (2) Adult patients with chronic phase (CP) and accelerated phase (AP) Ph+ CML resistant to or intolerant to prior therapy that included imatinib**

**Warnings:**

- **CI: hypokalemia, hypomagnesemia, long QT syndrome**
- **Myelosuppression, cardiac and arterial vascular occlusive events, pancreatitis and elevated serum lipase, hepatotoxicity, electrolyte abnormalities, tumor lysis syndrome, hemorrhage, fluid retention, effects on growth and development in pediatric patients, embryo-fetal toxicity, treatment discontinuations**

**Recommended Dosage:**

- **Newly diagnosed Ph+ CML-CP: 300 mg orally twice daily**
- **Resistant or intolerant Ph+ CML-CP and CML-AP: 400 mg orally twice daily**
- **Baseline Hepatic Impairment: Reduce dose**

**Availability:**

- **Capsules: 50 mg, 150 mg, and 200 mg**

# Oncology - Tyrosine Kinase Inhibitors – Oral

## cabozantinib (Cabometyx)

**March 2025 – FDA approved new indication for adult and pediatric patients ≥ 12 years old with previously treated, unresectable, locally advanced or metastatic, well-differentiated pancreatic neuroendocrine tumors (pNET) and well-differentiated extra-pancreatic neuroendocrine tumors (epNET)**

### FDA Indication:

- Treatment of patients with advanced renal cell carcinoma (RCC)
- Treatment of patients with advanced renal cell carcinoma, as a first-line treatment in combination with nivolumab
- Treatment of patients with hepatocellular carcinoma (HCC) who have been previously treated with sorafenib
- Treatment of adult and pediatric patients 12 years of age and older with locally advanced or metastatic differentiated thyroid cancer (DTC) that has progressed following prior VEGFR-targeted therapy and who are radioactive iodine-refractory or ineligible
- **Treatment of adult and pediatric patients 12 years of age and older with previously treated, unresectable, locally advanced or metastatic, well-differentiated pancreatic neuroendocrine tumors (pNET)**
- **Treatment of adult and pediatric patients 12 years of age and older with previously treated, unresectable, locally advanced or metastatic, well-differentiated extra-pancreatic neuroendocrine tumors (epNET)**

### Recommended Dosage:

- **Do not substitute Cabometyx tablets with cabozantinib capsules**
- **Dose is stratified by indication, age, and body weight, administered on an empty stomach**
- **Stop treatment 3 weeks prior to scheduled surgery, including dental surgery to reduce risk of hemorrhage and for ≥ 2 weeks after major surgery until adequate wound healing**

### Availability:

- Tablets: 60 mg, 40 mg, 20 mg

# Oncology - Tyrosine Kinase Inhibitors – Oral

## zanubrutinib (Brukinsa)

**June 2025 –FDA approved a new 160 mg oral tablet presentation**

**FDA Indication:**

- Treatment of adult patients with:
  - Mantle cell lymphoma (MCL) who have received at least one prior therapy*
  - Waldenström's macroglobulinemia (WM)
  - Relapsed or refractory marginal zone lymphoma (MZL) who have received at least one anti–CD20-based regimen*
  - Chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL)
  - Relapsed or refractory follicular lymphoma (FL), in combination with obinutuzumab, after two or more lines of systemic therapy*

* These indications are approved under accelerated approval; Continued approval for these indication may be contingent upon verification and description of clinical benefit in a confirmatory trial

**Recommended Dosage:**

- **160 mg orally twice daily or 320 mg orally once daily**
- **Tablets can be split in half; do not chew or crush**
- **Severe Hepatic Impairment: 80 mg orally twice daily**

**Availability:**

- **Tablets: 160 mg**
- Capsules: 80 mg

# 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

# Bone Resorption, IV
# Bone Resorption & Suppression Agents

## BONE DENSITY REGULATORS : RANK LIGAND INHIBITORS

# Disease State Description – Bone Density Regulators

## Osteoporosis

- Common metabolic bone disease causing low bone mass and tissue deterioration
- Affects > 12 million Americans and additional 43 million have low bone mass
- Fracture risk: ~1 in 2 women and 1 in 4 men in the United States (US) over 50 years old will have a related fracture
- Can occur in all racial groups but is most common in non-Hispanic white and Asian women
- Types:
  - **Postmenopausal**: Estrogen loss affects trabecular bone
  - **Age-related**: Affects both cortical and trabecular bone
  - **Secondary**: Caused by medications, diseases, or genetics

## American College of Physicians (ACP), 2025

- Pharmacologic Treatment of Primary Osteoporosis or Low Bone Mass to Prevent Fractures in Adults: A Living Clinical Guideline
- **First Line Therapy:** Bisphosphonates for males and postmenopausal females with primary osteoporosis
- **Second Line Therapy:** RANK ligand inhibitor (denosumab) for males and postmenopausal females with primary osteoporosis
- **High risk individuals (older postmenopausal women):** Sclerostin inhibitor (romosozumab) or recombinant PTH (teriparatide), followed by bisphosphonate therapy

# Bone Density Regulators

## denosumab-bmwo (Stoboclo)

### February 2025 – FDA approved a biosimilar to Prolia

**FDA Indication:**

- Treatment of postmenopausal women with osteoporosis at high risk for fracture
- Increase bone mass in men with osteoporosis at high risk for fracture
- Treatment of glucocorticoid-induced osteoporosis in men and women at high risk for fracture
- To increase bone mass in men at high risk for fracture receiving androgen deprivation therapy for nonmetastatic prostate cancer
- To increase bone mass in women at high risk for fracture receiving adjuvant aromatase inhibitor therapy for breast cancer

**Warnings:**

- BBW: Severe hypocalcemia in patients with advanced kidney disease
  - Evaluate for the presence of chronic kidney disease mineral and bone disorder (CKD-MBD) before starting therapy in patients with advanced chronic kidney disease, including dialysis patients
- CI: hypocalcemia, pregnancy

**Recommended Dosage:**

- 60 mg SQ every 6 months by a healthcare provider
- Take with calcium 1000 mg daily and at least 400 IU vitamin D daily

**Availability:**

- Injection: 60 mg/mL solution in a single-dose prefilled syringe

# Bone Density Regulators

## denosumab-bmwo (Osenvelt)

**February 2025 – FDA approved a biosimilar to Xgeva**

**FDA Indication:**

- Prevention of skeletal-related events in patients with multiple myeloma and in patients with bone metastases from solid tumors
- Treatment of adults and skeletally mature adolescents with giant cell tumor of bone that is unresectable or where surgical resection is likely to result in severe morbidity
- Treatment of hypercalcemia of malignancy refractory to bisphosphonate therapy

**Warnings:**

- CI: Hypocalcemia
- Osteonecrosis of the jaw, atypical femoral fracture, embryo-fetal toxicity

**Recommended Dosage:**

- Multiple Myeloma and Bone Metastasis from Solid Tumors: 120 mg SQ every 4 weeks by a healthcare provider
- Giant Cell Tumor of Bone or Hypercalcemia of Malignancy: 120 mg SQ every 4 weeks with additional 120 mg doses on Day 8 and 15 of the first month of therapy by a healthcare provider
- Take with calcium and vitamin D as needed to treat or prevent hypocalcemia

**Availability:**

- Injection: 120 mg/1.7 mL (70 mg/mL) solution in a single-dose vial

# 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

# 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

# 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)

- **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