Magellan Rx MANAGEMENT℠

Magellan Medicaid Administration

Washington Drug Utilization Review (DUR) Board Meeting

June 21st, 2023

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Agenda Topics

- Overview of Disease State
- Indications
- Dosage & Formulations
- Guideline Updates

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Stimulants and 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

- **Attention Deficit Hyperactivity Disorder (ADHD)**
  - The most common use of stimulants is for the treatment of ADHD, for which they are considered first-line therapy
  - ADHD, which has been diagnosed in approximately 9.8% of children 3 to 17 years of age and about 4% of adults, is a chronic condition with core symptoms of inattention, hyperactivity, and difficulty controlling behavior
  - It may also be accompanied by internalized disorders, such as sadness and anxiety, as well as aggressive and oppositional disorders
  - The 3 main types of ADHD are primary hyperactive, primary inattentive, and mixed

- **The Medical Letter, 2020**
  - Suggests that school-age children, adolescents, and adults begin with an oral stimulant, noting that none of the agents have shown to be more effective than another; however, some patients may respond better to amphetamines than to methylphenidate and vice versa
  - They advised that use of long-acting formulations, which generally contain both immediate- and extended-release components, has become standard clinical practice and the addition of a short-acting stimulants may improve symptom control early in the morning or to prolong the duration of action in the afternoon
  - While the alpha$_2$-agonists clonidine and guanfacine and the selective norepinephrine reuptake inhibitor atomoxetine can reduce ADHD symptoms, these agents are considered less effective than stimulants
  - Use of pitolisant and solriamfetol were not addressed Drugs for ADHD

Stimulants and Related Agents

- **amphetamine sulfate (Evekeo ODT)**
  - **October 2022: Evekeo ODT labeling has been revised to change the indication for the treatment of ADHD in pediatric patients 3-17 years of age to now include only patients 6-17 years of age. The 2.5 mg strength was previously indicated as a starting dose in patients 3-5 years of age. Labeling has been updated to remove all information related to the 2.5 mg strength. The 5 mg, 10 mg, 15 mg, and 20 mg ODTs remain available and are indicated for use in patients 6-17 years of age.**
  - **Indication**
    - **Indicated for the treatment of Attention Deficit Hyperactivity Disorder (ADHD) in pediatric patients 6 to 17 years of age**
  - **Warnings and Precautions**
    - Pregnancy: May cause fetal harm
    - Blood Pressure and Heart Rate Increases: Monitor blood pressure and pulse. Consider benefits and risks before use in patients for whom blood pressure increases may be problematic
    - Psychiatric Adverse Reactions: May cause psychotic or manic symptoms in patients with no prior history, or exacerbation of symptoms in patients with pre-existing psychosis. Evaluate for bipolar disorder prior to use
  - **Dosage**
    - Recommended starting dosage is 5 mg once or twice daily. If necessary, administer an additional dose after 4 to 6 hours. Titrate the dosage in increments of 5 mg at weekly intervals
  - **Availability**
    - **Orally disintegrating tablets: 5 mg, 10 mg, 15 mg, and 20 mg**

Stimulants and Related Agents

- **Drug Shortages**
  - **amphetamine mixed salts (Adderall)**
    - **October 2022:**
      - **The FDA has released shortage information for immediate release amphetamine mixed salts (Adderall) as Teva is currently experiencing ongoing intermittent manufacturing delays**
    - **May 2023:**
      - **FDA has updated its shortage information for amphetamine aspartate, amphetamine sulfate, dextroamphetamine saccharate, dextroamphetamine sulfate**
      - **Several manufacturers have product unavailable, with supply constraints, or on allocation**
      - **Teva has brand Adderall tablets available & limited supply of generic product**
  - **methamphetamine (Desoxyn)- March 2023**
    - **Both manufacturers of generic methamphetamine (Hikma & Mayne) are reporting product is currently unavailable**
    - **Estimated resolution by Mayne in September 2023**
    - **Brand Desoxyn remains available**

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Anti-Allergens, Oral

- ALLERGY : ALLERGENIC EXTRACTS / BIOLOGICALS - ORAL

Allergenic Extracts/Biologicals - Disease State Description

- **Allergic Rhinitis (hay fever)**
  - With or without allergic conjunctivitis, affects approximately 8% of adults and 9% of children in the United States
  - Allergen avoidance and medication therapy can provide significant symptom relief, but for many, symptoms remain
  - For some of these patients, allergen immunotherapy is a reasonable alternative
  - Subcutaneous immunotherapy (SCIT) has proven to be effective in the management of allergic rhinitis and asthma since the early twentieth century; however, it requires regular injections, typically over a period of 3 to 5 years, and carries the potential of serious systemic allergic reactions in response to the treatment itself

- **Peanut Allergies**
  - In 2010, an electronic survey of US homes estimated that 8% of children have food allergies
    - Estimated that peanut allergies, specifically, affect almost 1 million children in the US, and only 20% will outgrow their allergy
  - Previously, food allergy treatments primarily consisted of avoiding the allergen and promptly treating any accidental exposure
  - Reaction to peanut exposure varies from mild skin and/or gastrointestinal symptoms to severe angioedema and anaphylaxis
  - When accidental peanut exposure occurs, antihistamines can manage mild to moderate reactions, but patients must carry an epinephrine auto-injector to treat severe reactions
  - In January 2020, the FDA approved the first treatment for oral immunotherapy (OIT), Palforzia. OIT involves feeding an increasing amount of an allergen to a person allergic to that particular allergen
    - OIT does not cure a food allergy; rather, it induces a level of tolerance that prevents allergic reactions
    - Though Palforzia is an OIT agent, it has many similarities to the SLIT products in regard to safety, tolerability, and administration issues
    - Current guidelines on peanut allergy management from key stakeholder groups have not been updated yet to include Palforzia

Allergenic Extracts/Biologicals

- **house dust mite (Dermatophagoides farinae and dermatophagoides pteronyssinus) allergen extract (Odactra)**
  - **February 2023: FDA approved expanded indication for use as immunotherapy for house dust mite (HDM)-induced allergic rhinitis, with or without conjunctivitis, confirmed by in vitro testing for IgE antibodies or skin testing to include adolescents 12 to 17 years of age. Indication previously included only adults 18 to 65 years of age**
  - **Indication**
    - **Indicated as immunotherapy for the 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. ODACTRA is approved for use in persons 12 through 65 years of age**
  - **Warnings and Precautions**
    - BBW: Can cause anaphylaxis, which may be life-threatening and can occur at any time during therapy. Prescribe injectable epinephrine, instruct and train patients on its appropriate use, and instruct patients to seek immediate medical care upon its use. Do not administer to patients with uncontrolled asthma
  - **Dosage**
    - One tablet daily
  - **Availability**
    - Tablet, 12 SQ-HDM

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Antipsychotics

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

Antipsychotics – Disease State Description/Guidelines

Schizophrenia

- The most common psychotic illness is schizophrenia, which affects 1% of the population
- Between 25% and 50% of schizophrenic patients attempt suicide, and 10% of patients succeed in their attempt
- Symptoms include delusions, hallucinations, disorganized speech, disorganized or catatonic behavior, and negative symptoms, and at least 1 of these should be delusions, hallucinations, or disorganized speech

Diagnostic and Statistical Manual of Mental Disorders, 5th Edition; 2013

- American Academy of Child and Adolescent Psychiatry (AACAP), 2013
  - Recommend antipsychotic medication as primary treatment for schizophrenia spectrum disorders in children and adolescents
  - Recommend against the use of clozapine as a first-line agent (should be reserved for treatment-resistant patients), state that ziprasidone has not demonstrated efficacy in this population and is not FDA indicated for this population, and caution on its use with olanzapine due to weight gain
  - Ultimately, they state that the choice of which agent is based on FDA approval, adverse effect profile, patient and family preferences, provider comfort and/or familiarity, and cost
  - **As this practice parameter is more than 5 years old, it is considered an AACAP historical practice parameter; however, newer guidance is not available**

Antipsychotics – Guidelines

- American Psychiatric Association (APA), 2020
  - Since schizophrenia is a chronic illness that afflicts all aspects of life, the goals of treatment are to stabilize the patient (reduce acute symptoms) to return to baseline functioning, prevent recurrent of symptoms, and maximize functioning and quality of life
    - Goals may also be based on individual patient preferences impacting school, employment, and other quality of life-impacting components
  - Guidelines recommend that patients with schizophrenia be treated with an antipsychotic, including monitoring for both safety and efficacy
    - An antipsychotic should be continued in patients whose symptoms improve, with the APA suggesting that the same antipsychotic be used
    - They recommend clozapine specifically be used in patients with treatment-resistant schizophrenia and in patients with a significant risk of suicide
      - They also suggest clozapine for patients with aggressive behavior despite other treatments
    - A long-acting injectable is suggested for patients who prefer this therapy or for patients with a history of uncertain or poor adherence
  - Notably, the guidelines state that an evidence-based ranking or algorithm approach for antipsychotic selection is not practical due to clinical trial heterogeneity and limited comparative trials
  - In addition, there is no preference for first-generation antipsychotics (FGAs) or second-generation antipsychotics (SGAs), although clinically meaningful distinctions, such as tolerability, do occur
    - With the exception of clozapine, no antipsychotic has demonstrated superior efficacy when compared to other agents within the class
  - They also state that there is no reliable strategy to predict response; thus, initial treatment choice is often individualized and includes several patient-specific factors
  - The guideline also details management of adverse effects, such as acute dystonia, parkinsonism, akathisia, and tardive dyskinesia, some of which may warrant a switch to an alternative antipsychotic treatment

Antipsychotics – Disease State Description/Guidelines

Bipolar Disorder

- Lifelong prevalence estimates of bipolar disorder range from 0.9% to 2.1% of the population
- Characterized by episodes of mania, depression, or a mixed state
- Criterion used to diagnose bipolar I disorder is the presence of a manic episode (persistent elevated, expansive, or irritable mood for at least 1 week with increased energy/activity) or a mixed features specifier (rapidly alternating polarity of mood, sadness, irritability, and mania for at least 1 week), and 3 or more other characteristic symptoms
  - These symptoms include inflated self-esteem or grandiosity, decreased need for sleep, more talkative than usual or pressured speech, flight of ideas or feelings of racing thoughts, distractibility, increase in goal-directed activity or psychomotor agitation, and excessive involvement in risky, pleasurable activities

Diagnostic and Statistical Manual of Mental Disorders, 5th Edition; 2013

- American Psychiatric Association (APA), 2002
  - There is no cure for bipolar disorder, but the appropriate pharmacological treatment can decrease morbidity and mortality
  - First-line pharmacological treatment for more severe manic or mixed episodes requires the initiation of lithium or valproate plus an antipsychotic agent
    - SGAs are preferred over the FGAs due to their more tolerable adverse effect profile
  - For a bipolar manic episode with less severity, monotherapy with lithium, valproate, or an antipsychotic may be sufficient
  - Use of standard antidepressants as monotherapy can precipitate a manic episode in bipolar patients
  - During maintenance treatment, recommendations suggest to first optimize the medication dose in patients with bipolar disorder, especially in patients experiencing a breakthrough manic episode, and then consider adding another first-line agent
  - A Guideline Watch supplement was published in 2005 and included additional data on the use of SGAs (e.g., aripiprazole, olanzapine, quetiapine, risperidone, ziprasidone) as monotherapy or adjunctive therapy and an extended-release formulation of carbamazepine for the acute treatment of manic or mixed episodes and stated that these provide clinicians with additional treatment options

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Antipsychotics

- **FDA Communication**
  - **clozapine (Clozaril, Versacloz)**
    - **November 2022**
      - **FDA is temporarily exercising enforcement discretion with respect to certain clozapine REMS program requirements to ensure continuity of care for patients taking clozapine**
      - **FDA does not intend to object if pharmacists dispense clozapine without a REMS dispense authorization (RDA)**

- **Discontinuation**
  - **paliperidone ER (Invega)**
    - **February 2023**
      - **Janssen will discontinue manufacture of Invega 1.5 mg tablets**
      - **Generic versions of this strength are available. Invega 3 mg, 6 mg, & 9 mg tablets remain available**

Antipsychotics

- **cariprazine (Vraylar)**
  - **December 2022: The FDA approved a new indication for the adjunctive therapy to antidepressants for treatment of major depressive disorder (MDD) in adults**
    Indication
    - Treatment of schizophrenia in adults
    - Acute treatment of manic or mixed episodes associated with bipolar I disorder in adults
    - Treatment of depressive episodes associated with bipolar I disorder (bipolar depression) in adults
    - **Adjunctive therapy to antidepressants for the treatment of major depressive disorder (MDD) in adults**
  - **Warnings**
    - BBW: Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death. Not approved for the treatment of patients with dementia-related psychosis
    - Cerebrovascular Adverse Reactions in Elderly Patients with Dementia-Related Psychosis: Increased incidence of cerebrovascular adverse reactions (e.g., stroke, transient ischemic attack)
    - Pregnancy: May cause extrapyramidal and/or withdrawal symptoms in neonates with third trimester exposure
  - **Dosage**

	Starting Dose	Recommended Dose
Schizophrenia	1.5 mg daily	1.5 mg to 6 mg daily
Bipolar Mania	1.5 mg daily	3 mg to 6 mg daily
Bipolar Depression	1.5 mg daily	1.5 mg to 3 mg daily
Adjunctive therapy to antidepressants for MDD	**1.5 mg daily**	**1.5 mg to 3 mg daily**

  - **Availability**
    - **For extended-release injectable suspension: 12.5 mg, 25 mg, 37.5 mg, and 50 mg**

Antipsychotics

- **risperidone (Rykindo)**
  - **January 2023: The FDA has approved a new formulation for the atypical antipsychotic risperidone as an ER injectable suspension for IM use. The product is indicated for treatment of schizophrenia in adults, and as monotherapy or adjunctive therapy to lithium or valproate for maintenance treatment of Bipolar I Disorder in adults**
  - **Indication**
    - For the treatment of schizophrenia in adults
    - As monotherapy or as adjunctive therapy to lithium or valproate for the maintenance treatment of bipolar I disorder in adults
  - **Warnings**
    - BBW: Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death. Not approved for the treatment of patients with dementia-related psychosis
    - Cerebrovascular Adverse Reactions in Elderly Patients with Dementia-Related Psychosis: Increased incidence of cerebrovascular adverse reactions (e.g., stroke, transient ischemic attack)
    - Pregnancy: May cause extrapyramidal and/or withdrawal symptoms in neonates with third trimester exposure
  - **Dosage**
    - Recommended dosage is 25 mg intramuscular (IM) every 2 weeks. Patients not responding to 25 mg may benefit from 37.5 mg or 50 mg. Dosage titration should not be made more frequently than every 4 weeks.
    - The maximum recommended dosage should not exceed 50 mg every 2 weeks
    - Administer the first dose of Rykindo along with 7 days of oral risperidone
  - **Availability**
    - **For extended-release injectable suspension: 12.5 mg, 25 mg, 37.5 mg, and 50 mg**

Antipsychotics

- **risperidone (Uzedy)**
  - **April 2023: Risperidone extended-release injectable suspension has been approved for treatment of schizophrenia in adults. Uzedy will be available as 50 mg/0.14 mL, 75 mg/0.21 mL, 100 mg/0.28 mL, 125 mg/0.35 mL, 150 mg/0.42 mL, 200 mg/0.56 mL, & 250 mg/0.7 mL single-dose prefilled syringes**
  - **Indication**
    - **For the treatment of schizophrenia in adults**
  - **Warnings**
    - **BBW: Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death. Not approved for the treatment of patients with dementia-related psychosis**
    - **Cerebrovascular Adverse Reactions in Elderly Patients with Dementia-Related Psychosis: Increased incidence of cerebrovascular adverse reactions (e.g., stroke, transient ischemic attack)**
    - **Pregnancy: May cause extrapyramidal and/or withdrawal symptoms in neonates with third trimester exposure**
  - **Dosage**
    - Initiate Uzedy at the clinically appropriate dose using the following table:

Prior Oral Risperidone Therapy	Uzedy Dosage Once Monthly	Uzedy Dosage Once Every 2 Month
2 mg of oral risperidone per day	50 mg	100 mg
3 mg of oral risperidone per day	75 mg	150 mg
4 mg of oral risperidone per day	100 mg	200 mg
5 mg of oral risperidone per day	125 mg	250 mg

  - **Availability**
    - **Extended-release injectable suspension: 50 mg/0.14 mL, 75 mg/0.21 mL, 100 mg/0.28 mL, 125 mg/0.35 mL, 150 mg/0.42 mL, 200 mg/0.56 mL, and 250 mg/0.7 mL single-dose prefilled syringes**

Antipsychotics

- **aripiprazole (Abilify Asimtufii)**
  - **April 2023: Aripiprazole extended-release injectable suspension has been approved for treatment of schizophrenia in adults & as maintenance monotherapy for treatment of bipolar I disorder in adults. Product will be available as 720 mg/2.4 mL & 960 mg/3.2 mL single-dose prefilled syringes for IM use by a Healthcare Practitioner**
  - **Indication**
    - **For the treatment of schizophrenia in adults**
    - **As maintenance monotherapy treatment of bipolar I disorder in adults**
  - **Warnings**
    - **BBW: Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death. Not approved for the treatment of patients with dementia-related psychosis**
    - **Cerebrovascular Adverse Reactions in Elderly Patients with Dementia-Related Psychosis: Increased incidence of cerebrovascular adverse reactions (e.g., stroke, transient ischemic attack)**
    - **Pregnancy: May cause extrapyramidal and/or withdrawal symptoms in neonates with third trimester exposure**
  - **Dosage**
    - **For patients naïve to aripiprazole, establish tolerability with oral aripiprazole prior to initiating treatment**
    - **Recommended dosage is 960 mg administered once every 2 months as a single injection. Dose can be reduced to 720 mg in patients with adverse reactions**
  - **Availability**
    - **Extended-release injectable suspension: 960 mg/3.2 mL and 720 mg/2.4 mL single-dose pre-filled syringes**

Antipsychotics

- **brexpiprazole (Rexulti)**
  - **May 2023: FDA has approved a new indication for brexpiprazole for the treatment of agitation associated with dementia due to Alzheimer's disease (AD). The new indication carries a limitation of use stating it is not indicated as an as needed treatment for agitation associated with dementia due to AD**
  - **Indication**
    - Use as an adjunctive therapy to antidepressants for the treatment of major depressive disorder (MDD) in adults
    - Treatment of schizophrenia in adults and pediatric patients ages 13 years and older
    - **Treatment of agitation associated with dementia due to Alzheimer's disease**
    - **Limitations of Use: Not indicated as an as needed ("prn") treatment for agitation associated with dementia due to Alzheimer's disease**
  - **Warnings**
    - BBW: Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death. Not approved for the treatment of patients with dementia-related psychosis
    - Cerebrovascular Adverse Reactions in Elderly Patients with Dementia-Related Psychosis: Increased incidence of cerebrovascular adverse reactions (e.g., stroke, transient ischemic attack)
    - Pregnancy: May cause extrapyramidal and/or withdrawal symptoms in neonates with third trimester exposure
  - **Dosage**
    - **Alzheimer's:**
      - **Starting Dose: 0.5 mg/day**
      - **Recommended Target Dose: 2 mg/day**
      - **Maximum Dose: 3 mg/day**
  - **Availability**
    - Tablets: 0.25 mg, 0.5 mg, 1 mg, 2 mg, 3 mg, and 4 mg

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Ophthalmic Agents, Glaucoma

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

Glaucoma Agents - Disease State Description

- **Glaucoma**
  - Approximately 3 million people in the United States (US) suffer from glaucoma
    - It is the second most common cause of permanent blindness in the US. It is the leading cause of blindness among Hispanics and the second most common cause of blindness among African Americans
  - Increased intraocular pressure (IOP) is common in glaucoma and is believed to contribute to the damage to the optic nerve, which can lead to loss of visual sensitivity and field
  - However, some patients with glaucoma have normal IOP, and many patients with elevated IOP do not have glaucoma. IOP alone is no longer considered a diagnostic criterion for glaucoma
  - Two major types of glaucoma have been identified: open-angle and closed-angle
    - In open-angle glaucoma, there is reduced flow through the trabecular meshwork
      - Open-angle glaucoma accounts for the majority of cases
    - In closed-angle glaucoma, the iris is pushed forward against the trabecular meshwork, blocking fluid from escaping. Risk factors for the development of glaucoma include elevated IOP, advancing age (> 60 years), family history of glaucoma, and African American (> age 40 years) or Hispanic descent
- **Treatment**
  - The goal of treatment is to maintain the IOP in a range at which the optic nerve head and retinal nerve fiber layer are stable as well as preserve visual function and quality of life over their lifetime
  - Patients with primary open-angle glaucoma commonly have untreated IOP that is within the normal range (e.g., normal tension glaucoma); however, decreasing pressure is still beneficial in these patients

Glaucoma Agents

- **omidenepag isopropyl (Omlonti)**
  - **September 2022: FDA approved omidenepag isopropyl, a relatively selective prostaglandin E2 receptor agonist, for the reduction of elevated intraocular pressure in pts with open-angle glaucoma or ocular hypertension**
  - **Indication**
    - **A relatively selective prostaglandin E2 (EP2) receptor agonist, indicated for the reduction of elevated intraocular pressure (IOP) in patients with open-angle glaucoma or ocular hypertension**
  - **Warning/Precautions**
    - **Pigmentation**
    - **Eyelash changes**
    - **Ocular Inflammation**
    - **Macular Edema**
  - **Dosage**
    - **The recommended dosage is one drop in the affected eye(s) once daily in the evening**
  - **Availability**
    - **Ophthalmic solution containing 0.002% (0.02 mg/mL) of omidenepag isopropy**

Glaucoma Agents

- **latanoprost (Iyuzeh)**
  - December 2022: FDA approved Iyuzeh for the reduction of elevated intraocular pressure in patients with open-angle glaucoma or ocular hypertension
  - Indication
    - A prostaglandin F2α analogue indicated for the reduction of elevated intraocular pressure in patients with open-angle glaucoma or ocular hypertension
  - Warning/Precautions
    - Pigmentation
    - Eyelash changes
  - Dosage
    - The recommended dosage is one drop in the affected eye(s) once daily in the evening
  - Availability
    - Ophthalmic solution containing latanoprost 0.005% (50 mcg/mL)

- **brimonidine tartrate**
  - **January 2023:**
    - FDA has approved the first generic to Allergan's Alphagan P from Apotex
  - **March 2023:**
    - Apotex is voluntarily recalling 6 lots of brimonidine tartrate 0.15% ophthalmic solution due to cracks in some of the caps on bottles

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Thrombopoiesis Stimulating Factors

- HEMATOPOIETIC AGENTS : THROMBOPOIESIS (TPO) STIMULATING PROTEINS

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Ophthalmic Agents: Immunomodulators

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Idiopathic Pulmonary Fibrosis

- Respiratory Agents: Pulmonary Fibrosing Agents

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Smoking Cessation Agents

- Smoking Deterrents: Misc - Other

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Bone Resorption Inhibitors; Bone Resorption Suppression & Related Agents

-BONE DENSITY REGULATORS : RANK LIGAND INHIBITORS

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Growth Factors

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

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Growth Hormones

- ENDOCRINE AND METABOLIC AGENTS : GROWTH HORMONES

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Oncology, Oral – Prostate

- ONCOLOGY AGENTS : ANDROGEN BIOSYNTHESIS INHIBITORS – ORAL
- ONCOLOGY AGENTS : ANTIANDROGENS - ORAL

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Oncology, Oral – Hematologic

ONCOLOGY AGENTS : ANTINEOPLASTICS - MISC COMBINATIONS – ORAL
ONCOLOGY AGENTS : HEDGEHOG PATHWAY INHIBITORS – ORAL
ONCOLOGY AGENTS : MULTIKINASE INHIBITORS – ORAL
ONCOLOGY AGENTS : TYROSINE KINASE INHIBITORS – ORAL
ONCOLOGY AGENTS : HEDGEHOG PATHWAY INHIBITORS – ORAL
ONCOLOGY AGENTS : MULTIKINASE INHIBITORS – ORAL
ONCOLOGY AGENTS : TYROSINE KINASE INHIBITORS - ORAL

Oncology, Oral- Hematological - Overview of Disease State

- MULTIKINASE INHIBITORS- ORAL
  - Rydapt
  - Ukoniq
- PHOSPHATIDYLINOSITOL 3-KINASE (PI3K) INHIBITORS – ORAL
  - Copiktra
  - Zydelig
- PROTEASOME INHIBITORS – ORAL
  - Ninlaro
- RETINOIDS– ORAL
  - Tretinoin
- THALIDOMIDE ANALOGUES
  - **Lenalidomide**
  - Pomalidomide
  - Thalidomide
  - Pomalyst
  - Revlimid
- TYROSINE KINASE INHIBITORS – ORAL
  - Bosulif
  - **Brukinsa**
  - Calquence
  - Gleevec
  - Iclusig
  - Imatinib
  - **Imbruvica**
  - Scemblix
  - Sprycel
  - Tasigna
  - Xospata

Oncology, Oral- Hematological – Overview of Disease State

- **Graft versus Host Disease (GVHD)**
  - GVHD is an immune-mediated disease that can result following hematopoietic stem cell transplant (HSCT) when the transplanted cells (graft) recognize the recipient's body as foreign
    - Organ systems most commonly impacted by acute GVHD (aGVHD) include the skin, GI tract, and liver
  - Chronic GVHD (cGVHD) is generally an extension of acute GVHD that often develops more than 100 days after transplant, but it can also occur in those without acute GVHD. Symptoms include ocular manifestations (e.g., burning, irritation, photophobia, pain), oral or gastrointestinal (GI) manifestations (e.g., food sensitivity, oral dryness, pain, weight loss), respiratory manifestations (e.g., wheezing, dyspnea, cough), and neuromuscular manifestations (weakness, neuropathic pain, muscle cramps).

- **Treatment**
  - The American Society for Blood and Marrow Transplantation (re-named The American Society for Transplantation and Cellular Therapy [ASTCT] in 2019) published a clinical practice guideline in 2012 around the first- and second-line treatment of aGVHD
    - These guidelines state that corticosteroids are the standard of care for the initial treatment of aGVHD and note that the literature does not support the choice of any specific agent for secondary therapy of aGVHD
    - These guidelines were published prior to the May 2019 FDA approval of ruxolitinib (Jakafi) for the treatment of corticosteroid-refractory aGVHD in adult and pediatric patients ≥ 12 years of age
  - In 2019, the NCCN published their first set of clinical practice guidelines around hematopoietic cell transplantation (HCT)
    - The 3.2021 version of these guidelines recommend ruxolitinib as a category 1 option for patients with steroid-refractory aGVHD
  - The National Institutes of Health (NIH) recommend that corticosteroids are most commonly the initial systemic therapy choice for most patients with moderate to severe cGVHD
    - Adjunctive supportive care may also be used (e.g., artificial tears, artificial saliva). Ibrutinib was the first drug approved for cGVHD in patients who have failed ≥ 1 systemic treatment, but many other therapies have been used off-label and for primary or secondary therapy (e.g., low-dose methotrexate, mycophenolate mofetil [CellCept], sirolimus [Rapamune])
    - The NCCN 3.2021 guidelines list ibrutinib as a category 2A recommendation for steroid-refractory cGVHD along with multiple other agents also listed as category 2A recommendations

Oncology, Oral- Hematological – Overview of Disease State

- **Waldenström's macroglobulinemia**
  - Waldenström's macroglobulinemia/lymphoplasmacytic lymphoma (WM/LPL) is a B-cell disorder presenting as bone marrow infiltration with lymphoplasmacytic cells that are CD19+, CD20+, and CD22+
  - The 1.2022 NCCN guideline recommends treating only those patients who are symptomatic
    - These symptoms may include hyperviscosity, neuropathy, symptomatic adenopathy or organomegaly, amyloidosis, cryoglobulinemia, and cytopenias
    - Both zanubrutinib and ibrutinib with or without rituximab are listed as options for primary treatment (both category 1, preferred), while ixazomib combined with rituximab and dexamethasone is a category 2A, other recommended regimen for primary therapy
    - For patients who have received previous therapies for Waldenström's macroglobulinemia, zanubrutinib and ibrutinib with or without rituximab are category 1, preferred regimens. Acalabrutinib is a category 2A, other recommended treatment option
    - Up to 40% of WM patients may have recurrent mutations in the CXCR4 gene and certain CXCR4 mutations may confer resistance to ibrutinib; therefore, the NCCN guidelines recommend consideration of CXCR4 gene mutation testing for patients being initiated on ibrutinib therapy as a category 2A, useful in certain circumstances recommendation
  - No current US guidelines exist for the treatment of erythema nodosum leprosum, hypereosinophilic syndrome, or chronic eosinophilic leukemia

Oncology, Oral- Hematological – Overview of Disease State

- **Chronic Lymphocytic Leukemia (CLL) / Small Lymphocytic Lymphoma (SLL)**
  - CLL is classified as NHL and is the most prevalent adult leukemia in Western countries
  - It is generally a disease of the elderly, usually diagnosed around the age of 70 years
  - A small percentage of patients undergo Richter's transformation of their disease to an aggressive lymphoma
  - The treatment of CLL is highly individualized as some patients may only require observation and other patients may be candidates for cytotoxic or biologic therapies
  - CLL and SLL are different manifestations of the same disease
    - In CLL, a significant portion of the abnormal lymphocytes are in the blood as well as in the bone marrow
    - In SLL, there is a relative lack of abnormal lymphocytes in the blood; instead, abnormal lymphocytes are found predominantly in the lymph nodes, bone marrow, and other lymphoid tissues
  - In the 1950s and 1960s, alkylating agents, including chlorambucil (Leukeran) combined with corticosteroids, became the standard of care for patients requiring treatment for CLL. The role of chlorambucil in the current day management of CLL/SLL is combined with obinutuzumab (only if ≥ 65 years old or younger patient with significant comorbidities) for patients without del(17p)/TP53 mutation in patients who have indications for treatment (category 2A).

- **Treatment**
  - The NCCN V1.2023 first-line therapy recommendations include monotherapy with ibrutinib (Imbruvica) as another recommended regimen, category 1 recommendation for all CLL/SLL patients without del(17p)/TP53 regardless of age or comorbidities
  - Preferred regimens include acalabrutinib (Calquence) (with or without Obinutuzumab (Gazyva)) (category 1), venetoclax (Venclexta) plus Obinutuzumab (Gazyva) (category 1), and zanubrutinib (Brukinsa) (category 1) regardless of age or comorbidities for first-line therapy of patients without del(17p)/TP53

Oncology, Oral- Hematological – Overview of Disease State

- **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

- **Treatment**:
  - The 2022 B-cell lymphoma NCCN guidelines indicate that lenalidomide plus rituximab is one of several regimens that may be utilized for induction therapy when a less aggressive regimen is indicated
  - In the second-line setting, all BTK inhibitors, including acalabrutinib (Calquence), ibrutinib (Imbruvia), with or without rituximab, and zanubrutinib (Brukinsa), as well as lenalidomide plus rituximab (if BTK inhibitor is contraindicated), are listed as preferred options
  - The NCCN guidelines note that acalabrutinib and zanubrutinib have not been shown to be effective for ibrutinib-refractory MCL with BTK C481S mutations; however, patients with intolerance to ibrutinib have been successfully treated with acalabrutinib or zanubrutinib without recurrence of symptoms
  - Venetoclax with or without rituximab is a category 2A, useful in certain circumstances recommendation

Oncology, Oral- Hematological

- **New Generic**
  - **Lenalidomide- September 2022:**
    - **FDA approved first generic for Revlimid 2.5 mg and 20 mg capsules from Dr. Reddy's**

- **Manufacturer Communication**
  - **ibrutinib (Imbruvica) – April 2023:**
    - **The manufacturer of ibrutinib (Imbruvica), Abbvie, has announced plans to voluntarily withdraw the Accelerated Approvals for use in patients with mantle cell lymphoma (MCL) who have received ≥ 1 prior therapy and marginal zone lymphoma (MZL) who require systemic therapy and received ≥ 1 prior anti-CD20-based therapy**
    - **The other FDA-approved indications will remain as-is**
    - **The withdrawals are based on findings from the confirmatory trials for these uses, a requirement of the Accelerated Approvals**

Oncology, Oral- Hematological

- **zanubrutinib (Brukinsa)**
  - **January 2023: FDA has approved new indication for zanubrutinib for treatment of adults with CLL or SLL. Other previously existing indications include mantle cell lymphoma, Waldenström's macroglobulinemia, & marginal zone lymphoma**
  - **Indication**
    - Mantle cell lymphoma (MCL) who have received at least one prior therapy. This indication is approved under accelerated approval based on overall response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial
    - Waldenström's macroglobulinemia (WM)
    - Relapsed or refractory marginal zone lymphoma (MZL) who have received at least one anti–CD20-based regimen
    - This indication is approved under accelerated approval based on overall response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial
    - **Chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL)**
  - **Warning/Precautions**
    - Hemorrhage: Monitor for bleeding and manage appropriately
    - Infections: Monitor patients for signs and symptoms of infection, including opportunistic infections, and treat as needed
    - Cytopenias: Monitor complete blood counts during treatment
  - **Dosage**
    - **Recommended dosage: 160 mg orally twice daily or 320 mg orally once daily**
    - **Reduce dose in patients with severe hepatic impairment**
  - **Availability**
    - Capsules: 80 mg

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Oncology, Oral – Breast

ONCOLOGY AGENTS : ANTINEOPLASTICS - MISC COMBINATIONS – ORAL
ONCOLOGY AGENTS : CYCLIN DEPENDENT KINASES (CDK) INHIBITORS – ORAL
ONCOLOGY AGENTS : POLY (ADP-RIBOSE) POLYMERASE (PARP) INHIBITORS - ORAL
ONCOLOGY AGENTS : TYROSINE KINASE INHIBITORS - ORAL

Oncology, Oral- Breast – Overview of Disease State

- Breast cancer is the most common site of cancer for women in the United States (US), accounting for 30% of all cancer diagnoses, and is second only to lung cancer as a cause of cancer death in American women

- It is estimated that there will be 287,850 new cases of breast cancer diagnosed in the US in 2022 and there will be an estimated 43,500 deaths
  - The incidence of breast cancer in US women continues to increase by about 0.5% per year
  - Known risk factors that may be contributing to this increased incidence of breast cancer include a decline in fertility rates and an increase in body weight
  - Despite this increasing incidence, death rates from breast cancer have declined by 42% since 1989, largely due to improvements in both early detection and treatment
  - The overall 5-year survival for women diagnosed with breast cancer is 99%
  - Patients who present with localized disease have a 98.9% 5-year survival rate; however, prognosis for patients presenting with distant metastatic disease is much poorer, with a 5-year survival rate of only 29%
  - Breast cancer is most frequently diagnosed in women between the ages of 55 to 64 with the median age at diagnosis being 62 years

- Rarely, breast cancer may be diagnosed in men

- Other risk factors include various endocrine, genetic, environmental, and lifestyle factors

- Some of these risk factors are modifiable, some are not, and the impact of these factors are variable

Oncology, Oral- Breast – Guidelines

Neoadjuvant Treatment of Breast Cancer

- Historically, the role for neoadjuvant chemotherapy was limited to breast cancer patients with inoperable, locally advanced disease, but contemporary breast cancer treatment protocols now often include neoadjuvant therapy
- There are several reasons for this expanded role of neoadjuvant therapy
  - First, neoadjuvant therapy can increase the likelihood of patients being able to undergo breast-conserving surgery
  - Second, studies have shown that patients with triple-negative breast cancer (TNBC) and those with HER2-positive disease who achieve a pathologic complete response (pCR), defined as the absence of invasive disease in the breast and lymph nodes, following neoadjuvant therapy have an improved prognosis
- Recently, published research has focused on response to neoadjuvant treatment as a predictive marker and a guide for selecting subsequent adjuvant therapy

- **ASCO Guidelines, 2021**
  - Regarding neoadjuvant chemotherapy, endocrine therapy, and targeted therapy recommends neoadjuvant therapy with any of these modalities if the patient has inflammatory breast cancer or if the patient has unresectable or locally advanced disease at presentation such that the disease may be rendered resectable with neoadjuvant treatment
  - Furthermore, the ASCO guideline states neoadjuvant systemic therapy should be offered to patients with high-risk TNBC in whom the finding of residual disease at time of surgery would guide recommendations related to adjuvant therapy
  - Regarding neoadjuvant endocrine therapy, the ASCO guideline states that postmenopausal patients with HR-positive/HER2-negative disease may receive a neoadjuvant aromatase inhibitor (AI) therapy to increase locoregional treatment options, or if there is no intent for surgery, endocrine therapy may be used for disease control
  - However, for premenopausal patients with HR-positive/HER2-negative early-stage diseases, neoadjuvant endocrine therapy should not be routinely offered outside of a clinical trial

Oncology, Oral- Breast

- ONCOLOGY AGENTS : ANTINEOPLASTICS - MISC COMBINATIONS – ORAL
  - Kisqali
  - Femara

- ONCOLOGY AGENTS : CYCLIN DEPENDENT KINASES (CDK) INHIBITORS – ORAL
  - **Ibrance**
  - Kisqali
  - **Verzenio**

- ONCOLOGY AGENTS : POLY (ADP-RIBOSE) POLYMERASE (PARP) INHIBITORS – ORAL
  - Lynparza
  - Rubraca
  - Talzenna

- ONCOLOGY AGENTS : TYROSINE KINASE INHIBITORS – ORAL
  - Lapatinib
  - Nerlynx
  - **Tukysa**
  - Tykerb

Oncology, Oral- Breast

- **palbociclib (Ibrance)**
  - **December 2022: FDA expanded the indication for 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 has been expanded to include pre- and perimenopausal women**
  - **Indication**
    - The treatment of adult patients with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer in combination with:
      - **An aromatase inhibitor as initial endocrine-based therapy (1);** or
      - Fulvestrant in patients with disease progression following endocrine therapy
  - **Warnings**
    - Neutropenia: Monitor complete blood count prior to start of therapy and at the beginning of each cycle, as well as on Day 15 of the first 2 cycles, and as clinically indicated
    - Embryo-Fetal Toxicity: Can cause fetal harm. Advise patients of potential risk to a fetus and to use effective contraception
  - **Dosage**
    - Recommended starting dose: 125 mg once daily taken with food for 21 days followed by 7 days off treatment
  - **Availability**
    - Capsules: 125 mg, 100 mg, and 75 mg

Oncology, Oral- Breast

- **tucatinib (Tukysa)**
  - **January 2023: FDA has approved new indication for tucatinib in combination with trastuzumab for treatment of adults with RAS wild-type, HER2-positive unresectable or metastatic colorectal cancer that has progressed following treatment with fluoropyrimidine-, oxaliplatin-, & irinotecan-based chemotherapy**
  - **Indication**
    - In combination with trastuzumab and capecitabine for treatment of adult patients with advanced unresectable or metastatic HER2-positive breast cancer, including patients with brain metastases, who have received one or more prior anti-HER2-based regimens in the metastatic setting
    - **In combination with trastuzumab for the treatment of adult patients with RAS wild-type HER2-positive unresectable or metastatic colorectal cancer that has progressed following treatment with fluoropyrimidine-, oxaliplatin-, and irinotecan-based chemotherapy**
      - **This indication is approved under accelerated approval based on tumor response rate and durability of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials**
  - **Warnings**
    - Hepatotoxicity: Monitor ALT/AST/Bilirubin prior to starting and every 3 weeks during treatment
    - Embryo-Fetal Toxicity: Can cause fetal harm. Advise patients of potential risk to a fetus and to use effective contraception
  - **Dosage**
    - In patients with unresectable or metastatic colorectal cancer, confirm the presence of HER2 protein overexpression and RAS wild-type in tumor specimens prior to the initiation of treatment
    - **Recommended dosage: 300 mg taken orally twice daily with or without food**
    - For patients with severe hepatic impairment, the recommended dosage is 200 mg orally twice daily
  - **Availability**
    - Tablets: 50 mg and 150 mg

Oncology, Oral- Breast

- **abemaciclib (Verzenio)**
  - **March 2023: Abemaciclib's indication has been expanded to include (1) use in combination with endocrine therapy (tamoxifen or an aromatase inhibitor) for the adjuvant treatment of adult patients with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative, node-positive, early breast cancer at high risk of recurrence. Previously, it was only indicated for use in these patients with a Ki-67 score ≥20% as determined by an FDA-approved test; and (2) in combination with an aromatase inhibitor as initial endocrine based therapy for the treatment of adult patients with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer; previously, this indication was only for treatment of postmenopausal women and men**
  - **Indication**
    - **In combination with endocrine therapy (tamoxifen or an aromatase inhibitor) for the adjuvant treatment of adult patients with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative, node-positive, early breast cancer at high risk of recurrence**
    - In combination with an aromatase inhibitor as initial endocrinebased therapy for the treatment of adult patients with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer
    - In combination with fulvestrant for the treatment of adult patients with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer with disease progression following endocrine therapy
    - As monotherapy for the treatment of adult patients with HRpositive, HER2-negative advanced or metastatic breast cancer with disease progression following endocrine therapy and prior chemotherapy in the metastatic setting
  - **Dosage**
    - **Recommended starting dose in combination with fulvestrant, tamoxifen, or an aromatase inhibitor: 150 mg twice daily**
    - **Recommended starting dose as monotherapy: 200 mg twice daily**
  - **Availability**
    - Tablets: 50 mg, 100 mg, 150 mg, and 200 mg

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Oncology, Oral – Other

- ONCOLOGY AGENTS : ANTINEOPLASTICS - MISC COMBINATIONS – ORAL
- ONCOLOGY AGENTS : FGFR KINASE INHIBITORS – ORAL
- ONCOLOGY AGENTS : MEK INHIBITORS – ORAL
- ONCOLOGY AGENTS : MULTIKINASE INHIBITORS – ORAL
- ONCOLOGY AGENTS : POLY (ADP-RIBOSE) POLYMERASE (PARP) INHIBITORS – ORAL
- ONCOLOGY AGENTS : TROPOMYOSIN RECEPTOR KINASE INHIBITORS – ORAL
- ONCOLOGY AGENTS : TYROSINE KINASE INHIBITORS - ORAL

Oncology, Oral- Other

- ONCOLOGY AGENTS : ANTINEOPLASTICS - MISC COMBINATIONS – ORAL
  - Lonsurf
- ONCOLOGY AGENTS : FGFR KINASE INHIBITORS – ORAL
  - Balversa
  - **Lytgobi**
  - **Pemazyre**
  - Truseltiq
- ONCOLOGY AGENTS : MEK INHIBITORS – ORAL
  - Koselugo
- ONCOLOGY AGENTS : MULTIKINASE INHIBITORS – ORAL
  - Stivarga
- ONCOLOGY AGENTS : POLY (ADP-RIBOSE) POLYMERASE (PARP) INHIBITORS – ORAL
  - Lynparza
  - **Rubraca**
  - **Zejula**
- ONCOLOGY AGENTS : TROPOMYOSIN RECEPTOR KINASE INHIBITORS – ORAL
  - Vitrakvi
- ONCOLOGY AGENTS : TYROSINE KINASE INHIBITORS – ORAL
  - Ayvakit
  - Caprelsa
  - Cometriq
  - **Jaypirca**
  - Qinlock
  - **Turalio**

Oncology, Oral- Other

- **Cholangiocarcinoma**
  - Tumors originating in the epithelium of the bile duct
  - They are typically classified as either intrahepatic or extrahepatic, depending on their location within the biliary tree
  - Cholangiocarcinoma is rare in the US, where about 8,000 people are diagnosed each year
  - This may be an underestimate of the actual number of cases because these cancers can be difficult to diagnose and may often be classified as other types of cancer such as hepatocellular carcinoma or cancer of unknown origin
  - The average age at diagnosis is between 70 and 72 years of age. Treatment includes a surgical consultation to assess if the patient is a candidate for resection or possible organ transplantation
  - For patients with unresectable or metastatic disease, there is an increasing role for molecular profiling. Intrahepatic cholangiocarcinoma harbors IDH1/2 mutations in 10% to 23% of cases and mutations in FGFR2 fusions occur in 13% to 14%
  - The prognostic significance of IDH1/2 mutations in intrahepatic cholangiocarcinoma is unclear, but FGFR mutations may improve prognosis. Additionally, these mutations provide an opportunity for targeted therapies

- **Treatment (NCCN Guidelines, 1.2022)**
  - The NCCN guidelines on hepatobiliary cancers, version 1.2022, include infigratinib as a potential therapeutic regimen in the subsequent-line therapy setting for biliary tract cancers if disease has progressed on or after systemic treatment for unresectable or metastatic disease
  - Infigratinib is listed specifically as a regimen for being useful in certain circumstances for cholangiocarcinoma with FGFR2 fusions or rearrangements (category 2A recommendation)
  - Pemigatinib is also recommended (category 2A) for these patients

Oncology, Oral- Other

- **futibatinib (Lytgobi)**
  - **January 2023: FDA approved futibatinib, a fibroblast growth factor receptor (FGFR) inhibitor, for adult patients with previously treated, unresectable, locally advanced or metastatic intrahepatic cholangiocarcinoma harboring FGFR2 gene fusions or other rearrangements. Continued approval is based upon confirmation of clinical benefit**
  - **Indication**
    - **The treatment of adult patients with previously treated, unresectable, locally advanced or metastatic intrahepatic cholangiocarcinoma harboring fibroblast growth factor receptor 2 (FGFR2) gene fusions or other rearrangements**
    - **This indication is approved under accelerated approval based on overall response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s)**
  - **Warnings**
    - **Ocular Toxicity: Can cause retinal pigment epithelial detachment (RPED). Perform a comprehensive ophthalmological examination including optical coherence tomography (OCT) prior to initiation of therapy, every 2 months for the first 6 months, and every 3 months thereafter and urgently at any time for visual symptoms**
    - **Embryo-Fetal Toxicity: Can cause fetal harm. Advise patients of reproductive potential of the potential risk to the fetus and to use effective contraception**
  - **Dosage**
    - **Confirm the presence of an FGFR2 gene fusion or other rearrangement prior to initiation of treatment with Lytgobi**
    - **Recommended dose is 20 mg orally (five 4 mg tablets) once daily until disease progression or unacceptable toxicity occurs**
  - **Availability**
    - **Tablets: 4 mg**

Oncology, Oral- Other

- **Ovarian Cancer**
  - Ovarian cancer is the fifth most common cause of cancer-related death in women in the US
  - The risk of ovarian cancer increases with age, and the median age at diagnosis is 63 years and 5-year survival is 49.7%
  - More than half of patients present with advanced disease
  - Ovarian cancer has been shown to have a higher prevalence in families with BRCA1 or BRCA2 genotypes and, in these patients, the onset of disease is usually at a younger age; however, patients with these mutations account for only 15% of all ovarian cancers

Oncology, Oral- Other

- **Treatment (NCCN Guidelines, 1.2022)**
  - Primary treatment for advanced ovarian cancer usually begins with cytoreductive surgery to remove as much gross disease as possible because patients with more complete debulking have better outcomes
  - The majority of patients, excluding those with very early stage disease, are recommended to receive postoperative, adjuvant systemic chemotherapy
  - Recommended protocols generally include a taxane (paclitaxel or docetaxel) and a platinum agent (cisplatin or carboplatin)
  - Intraperitoneal chemotherapy is recommended in addition to intravenous chemotherapy in certain clinical situations
  - A newer class of orally targeted agents, the poly ADP-ribose polymerase (PARP) inhibitors, also are available for the treatment of ovarian cancer
  - There are currently 3 FDA-approved PARP inhibitors approved for use in ovarian cancer on the market including niraparib (Zejula), olaparib (Lynparza), and rucaparib (Rubraca)
    - Olaparib was the first PARP inhibitor approved by the FDA in late 2014, and approval was limited to patients who had a germline BRCA mutation, advanced disease, and received
      ≥ 3 previous lines of chemotherapy; this indication was withdrawn in August of 2022
    - Since that time, the FDA-approved indications and the role of PARP inhibitors in ovarian cancer has expanded
    - Selection of patients with advanced ovarian cancer who have a high likelihood of responding to PARP inhibitors has also been expanded to include patients identified as being homologous recombination status (HR)-positive
  - HR positivity is defined as having either a deleterious BRCA mutation (germline or somatic) and/or a genomic instability as identified by an appropriate test
  - Niraparib is approved for patients who have received ≥ 3 prior lines of therapy and whose cancer is associated with HR positive status, while rucaparib is approved for patients who have received ≥ 2 lines of chemotherapy and have an identified deleterious BRCA mutation (germline and/or somatic)

Oncology, Oral- Other

- **niraparib (Zejula)**
  - **December 2022: Indication for maintenance treatment of recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer has been restricted to only pts with deleterious or suspected deleterious germline BRCA-mutated cancer who are in complete or partial response to platinum-based chemotherapy**
  - **April 2023: FDA approved use of Zejula (niraparib) 100 mg, 200 mg, and 300 mg tablets for: (1) maintenance treatment of adults with advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in a complete or partial response to first-line platinum-based chemotherapy; and (2) maintenance treatment of adults with deleterious or suspected deleterious germline BRCA-mutated recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in a complete or partial response to platinum-based chemotherapy**
  - **Indication**
    - Maintenance treatment of adult patients with advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in a complete or partial response to first-line platinum based chemotherapy
    - **For the maintenance treatment of adult patients with deleterious or suspected deleterious germline BRCA-mutated recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in a complete or partial response to platinum-based chemotherapy. Select patients for therapy based on an FDA-approved companion diagnostic for Zejula**
  - **Warnings**
    - Embryo-Fetal Toxicity: Can cause fetal harm. Advise patients of reproductive potential of the potential risk to the fetus and to use effective contraception
  - **Dosage**
    - First-line maintenance treatment of advanced ovarian cancer:
      - For patients weighing < 77 kg OR with a platelet count <150,000/mcL, the recommended dosage is 200 mg taken orally once daily
      - For patients weighing ≥ 77 kg AND a platelet count ≥ 150,000/mcL, the recommended dosage is 300 mg taken orally once daily
  - **Availability**
    - Capsules: 100 mg

Oncology, Oral- Other

- **rucaparib camsylate (Rubraca)**
  - **December 2022: Indication for maintenance treatment of recurrent ovarian cancer has been restricted to pts with a deleterious BRCA mutation (germline and/or somatic). Statement added that an FDA-approved test for the detection of deleterious germline and/or somatic BRCA mutations is not currently available. MDS/AML section of Warnings and Precautions updated to include data in patients with BRCA-mutated recurrent ovarian cancer**
  - **Indication**
    - **Ovarian cancer:**
      - **For the maintenance treatment of adult patients with a deleterious BRCA mutation (germline and/or somatic)- associated recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in a complete or partial response to platinum-based chemotherapy**
    - Prostate cancer
      - For the treatment of adult patients with a deleterious BRCA mutation (germline and/or somatic)-associated metastatic castration-resistant prostate cancer (mCRPC) who have been treated with androgen receptor-directed therapy and a taxane-based chemotherapy. Select patients for therapy based on an FDA-approved companion diagnostic. This indication is approved under accelerated approval based on objective response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials
  - **Warnings**
    - Embryo-Fetal Toxicity: Can cause fetal harm. Advise patients of reproductive potential of the potential risk to the fetus and to use effective contraception
  - **Dosage**
    - Recommended dose is 600 mg orally twice daily with or without food
    - Continue treatment until disease progression or unacceptable toxicity
  - **Availability**
    - Tablets: 200 mg, 250 mg, and 300 mg

Oncology, Oral- Other

- **pemigatinib (Pemazyre)**
  - **September 2022: FDA approved a new indication for the treatment of adults with relapsed or refractory myeloid/lymphoid neoplasms (MLNs) with fibroblast growth factor receptor (FGFR) 1 rearrangement**
  - **Indication**
    - For the treatment of adults with previously treated, unresectable locally advanced or metastatic cholangiocarcinoma with a fibroblast growth factor receptor 2 (FGFR2) fusion or other rearrangement as detected by an FDA-approved test
    - This indication is approved under accelerated approval based on overall response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s)
    - **For the treatment of adults with relapsed or refractory myeloid/lymphoid neoplasms (MLNs) with FGFR1 rearrangement**
  - **Warnings**
    - Embryo-Fetal Toxicity: Can cause fetal harm. Advise patients of reproductive potential of the potential risk to the fetus and to use effective contraception
    - Ocular Toxicity: Can cause retinal pigment epithelial detachment. Perform ophthalmological examination including optical coherence tomography (OCT) prior to initiation of therapy, every 2 months for the first 6 months of treatment and every 3 months thereafter, and urgently at any time for visual symptoms
  - **Dosage**
    - **Myeloid/lymphoid neoplasms with FGFR1 rearrangement: Recommended dosage is 13.5 mg orally once daily. Continue treatment until disease progression or unacceptable toxicity**
    - All other dosages can be found in PI/TCR
  - **Availability**
    - Tablets: 4.5 mg, 9 mg, and 13.5 mg

Oncology, Oral- Other

- **pexidartinib (Turalio)**
  - **October 2022: The approved dosage has changed from 400 mg twice daily on an empty stomach to 250 mg twice daily with a low-fat meal. The approved dosage form is now 125 mg capsules; 200 mg capsules are no longer approved**
  - **Indication**
    - The treatment of adult patients with symptomatic tenosynovial giant cell tumor (TGCT) associated with severe morbidity or functional limitations and not amenable to improvement with surge
  - **Warnings**
    - BBW: Can cause serious and potentially fatal liver injury.
    - Renal Impairment: Reduce the dosage for patients with mild to severe renal impairment
    - Hepatic Impairment: Reduce the dosage for patients with moderate hepatic impairment
    - Embryo-Fetal Toxicity: Can cause fetal harm. Advise patients of reproductive potential of the potential risk to the fetus and to use effective contraception
    - Potential Risks Associated with a High-Fat Meal: May increase incidence and severity of adverse reactions, including hepatotoxicity. Avoid taking TURALIO with a high-fat meal (approximately 55 to 65 grams of total fat)
  - **Dosage**
    - Recommended Dosage: 250 mg orally twice daily with a low-fat meal (approximately 11 to 14 grams of total fat)
  - **Availability**
    - **Capsules: 125 mg**

Oncology, Oral- Other

- **pirtobrutinib (Jaypirca)**
  - **January 2023: FDA granted Accelerated Approval to pirtobrutinib, a kinase inhibitor indicated for the treatment of adults with r/r mantle cell lymphoma after ≥ 2 lines of systemic therapy, including a BTK inhibitor**
  - **Indication**
    - **The treatment of adult patients with relapsed or refractory mantle cell lymphoma (MCL) after at least two lines of systemic therapy, including a BTK inhibitor**
    - **This indication is approved under accelerated approval based on response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial**
  - **Warnings**
    - **Embryo-Fetal Toxicity: Can cause fetal harm. Advise patients of reproductive potential of the potential risk to the fetus and to use effective contraception**
    - **Infections: Monitor for signs and symptoms of infection, evaluate promptly, and treat**
    - **Hemorrhage: Monitor for bleeding and manage appropriately**
    - **Cytopenias: Monitor complete blood counts during treatment**
    - **Atrial Fibrillation and Atrial Flutter: Monitor for symptoms of arrhythmias and manage appropriately**
  - **Dosage**
    - **Recommended dosage: 200 mg orally once daily; swallow whole with water, with or without food**
    - **Manage toxicity using treatment interruption, dosage reduction, or discontinuation**
  - **Availability**
    - **Tablets: 50 mg, 100 mg**

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Oncology, Oral – Lung

- ONCOLOGY AGENTS : TOPOISOMERASE INHIBITORS – ORAL
- ONCOLOGY AGENTS : TROPOMYOSIN RECEPTOR KINASE INHIBITORS – ORAL
- ONCOLOGY AGENTS : TYROSINE KINASE INHIBITORS - ORAL

Oncology, Oral- Lung – Overview of Disease State

- Lung cancer is the leading cause of cancer death in both men and women in the United States (US)
  - In 2023, an estimated 238,340 new cases of lung cancer will be diagnosed, and 127,070 deaths are estimated to occur
  - Currently, 5-year survival is estimated to be 23%, an increase from 15% reported in 2019
  - Declines in lung cancer mortality in the US have been accelerating in recent years
  - From 2005 through 2014, lung cancer mortality declined 3.1%, but from 2014 through 2020, this decline more than doubled, resulting in a 5.3% decline in lung cancer mortality over that period
  - Additionally, there has been a steady decline in the incidence of lung cancer diagnoses in the US; the number of diagnoses declined 2.3% in the most recent measurement
  - Despite these encouraging trends, there are still more US lung cancer deaths annually than deaths from breast cancer, prostate cancer, and colorectal 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 carcinogenic chemicals in cigarette smoke are responsible for most lung cancer-related deaths, while exposure to second-hand smoke also results in an increased relative risk of developing lung cancer

- While chemoprevention agents are not yet established, lung cancer screening using low-dose computerized tomography (LDCT) is recommended by the US Preventive Services Task Force (USPSTF), who expanded their lung cancer screening guidelines in 2021
  - The USPSTF guidelines now recommend annual screening with LDCT for patients 50 to 80 years of age who are current smokers with at least a 20 pack-year smoking history and former smokers who have quit within the past 15 years

Oncology, Lung – Guidelines

- **EGFR sensitizing mutations**
  - NCCN guidelines
    - Have been updated to incorporate the use of osimertinib (Tagrisso) in the adjuvant setting of earlier stage NSCLC
    - The guidelines recommend the use of osimertinib with stage 1B to 3A disease who have undergone complete resection with EGFR exon 19 deletions or exon 21 L858R mutation disease who received previous adjuvant chemotherapy or are ineligible to receive platinum-based chemotherapy
    - For patients with EGFR exon 20 insertion positive metastatic disease with disease progression, NCCN recommends mobocertinib (Exkivity) as an option for subsequent therapy
  - ASCO/Ontario Health (Cancer Care Ontario) Guidelines, 2023
    - Regarding stage 4 NSCLC with driver mutations
    - Indicate that osimertinib should be offered in the first-line setting for patients with T790M, L858R, or exon 19 deletion EGFR mutations
    - If osimertinib is not available in the first-line setting, gefitinib with chemotherapy or dacomitinib may be offered
    - Other options listed by the ASCO guidelines include afatinib or erlotinib/bevacizumab; erlotinib/ramucirumab; or gefitinib, erlotinib, or icotinib (not available in the US) as single agents
- ***BRAF V600E point mutations***
  - For patients with advanced or metastatic lung cancer who are found to have a BRAF V600E mutation, a combination of dabrafenib (Tafinlar) plus trametinib (Mekinist) is recommended as preferred first-line therapy by NCCN, while single agent vemurafenib (Zelboraf) may be an option if the combination of dabrafenib plus trametinib is not tolerated
  - According to ASCO guidelines
    - Patients with stage 4 NSCLC and BRAF V600E mutations should be offered dabrafenib/trametinib in the first-line setting
    - For patients who receive targeted therapy in the first-line setting, second-line therapy should consist of standard nondriver mutation guideline recommendations

Oncology, Lung – Guidelines

- ***MET exon 14 skipping mutations***
  - Both capmatinib (Tabrecta) and tepotinib (Tepmetko) are listed as NCCN category 2A, preferred options, while crizotinib (Xalkori) is classified as a category 2A, useful in certain circumstances recommendation
  - ASCO guidelines recommend offering capmatinib or tepotinib in the first-line setting
  - If the patient does not receive one of these therapies in the first-line setting, it may be offered in the second-line setting

- ***ALK rearrangements***
  - ASCO 2021 updated guidelines regarding patients with stage 4 NSCLC who harbor an ALK rearrangement recommend that alectinib or brigatinib be offered in the first-line setting
    - The guidelines recommend that if alectinib and brigatinib are not available, patients should be offered ceritinib or crizotinib
    - The ASCO guidelines also outline drug choices for the second-line setting
    - Lorlatinib in the second-line setting is recommended if the patient received alectinib or brigatinib in the first-line setting
    - If the patient received crizotinib in the first-line setting, then alectinib, brigatinib, or ceritinib should be offered
    - In the third-line setting, lorlatinib may be offered

- ***ROS1 rearrangements***
  - ASCO guidelines recommend crizotinib or entrectinib in the first-line setting
  - Other options include ceritinib or lorlatinib
  - If targeted therapy was given in the first-line setting, then ASCO guidelines recommend that the standard treatment based on nondriver mutation guidelines should be followed

Oncology, Lung – Guidelines

- ***RET rearrangements***
  - Both pralsetinib (Gavreto) and selpercatinib (Retevmo) are listed as NCCN category 2A, preferred first-line options
  - ASCO guidelines state that selpercatinib or standard therapy based on nondriver mutation guidelines may be offered in the first-line setting
  - At the time of the ASCO publication, the pralsetinib recommendation in the first-line setting was provisional, pending confirmatory data
  - Recommendations for second-line setting for RET rearrangements are dependent on the therapy received in the first-line; if targeted therapy with pralsetinib or selpercatinib were not given in the first-line setting, they may be offered as second-line therapy

- ***NTRK fusions***
  - Both entrectinib (Rozlytrek) and larotrectinib (Vitrakvi) are NCCN category 2A preferred options in the first-line setting
  - ASCO guidelines also recommend entrectinib or larotrectinib in this setting, and these drugs may also be offered in the second-line setting for patients with NTRK gene fusions who did not receive them in the first-line setting

Oncology, Oral- Lung

- ONCOLOGY AGENTS : TOPOISOMERASE INHIBITORS – ORAL
  - Hycamtin

- ONCOLOGY AGENTS : TROPOMYOSIN RECEPTOR KINASE INHIBITORS – ORAL
  - Rozlytrek

- ONCOLOGY AGENTS : TYROSINE KINASE INHIBITORS – ORAL
  - Alecensa
  - Alunbrig
  - Erlotinib
  - Exkivity
  - Gavreto
  - **Gefitinib**
  - Gilotrif
  - Iressa
  - Lorbrena
  - **Retevmo**
  - Tabrecta
  - Tagrisso
  - Tarceva
  - Vizimpro
  - Xalkori
  - Zykadia

Oncology, Oral- Lung

- **selpercatinib (Retevmo)**
  - **September 2022: The FDA has granted Accelerated Approval to selpercatinib for adults with locally advanced or metastatic solid tumors with a rearranged during transfection (RET) gene fusion that have progressed on or following prior systemic treatment or who have no satisfactory alternative treatment options. Selpercatinib is also indicated for certain patients with RET fusion-positive NSCLC, RET-mutant medullary thyroid cancer, and RET fusion-positive thyroid cancer**
  - **Indication**
    - Adult patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) with a rearranged during transfection (RET) gene fusion, as detected by an FDA-approved test
    - Adult and pediatric patients 12 years of age and older with advanced or metastatic medullary thyroid cancer (MTC) with a RET mutation, as detected by an FDA-approved test, who require systemic therapy
    - Adult and pediatric patients 12 years of age and older with 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)
    - **Adult patients with locally advanced or metastatic solid tumors with a RET gene fusion that have progressed on or following prior systemic treatment or who have no satisfactory alternative treatment options**
  - **Dosage**
    - Select patients for treatment with RETEVMO based on the presence of a RET gene fusion (NSCLC, thyroid, or other solid tumors) or specific RET gene mutation (MTC)
    - Recommended dosage in adults and pediatric patients 12 years of age or older is based on weight
      - Less than 50 kg: 120 mg orally twice daily
      - 50 kg or greater: 160 mg orally twice daily
    - Reduce dose in patients with severe hepatic impairment
  - **Availability**
    - Capsules: 40 mg, 80 mg

Oncology, Oral- Lung

- **gefitinib**
  - **The FDA has approved the first generic to AstraZeneca's Iressa from Apotex**

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Oncology, Oral – Renal Cell Carcinoma

- ONCOLOGY AGENTS : MTOR KINASE INHIBITORS – ORAL
- ONCOLOGY AGENTS : MULTIKINASE INHIBITORS – ORAL
- ONCOLOGY AGENTS : TYROSINE KINASE INHIBITORS - ORAL

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Oncology, Oral – Skin

- ONCOLOGY AGENTS : BRAF KINASE INHIBITORS – ORAL
- ONCOLOGY AGENTS : HEDGEHOG PATHWAY INHIBITORS – ORAL
- ONCOLOGY AGENTS : MEK INHIBITORS - ORAL

Oncology, Oral- Skin– Overview of Disease State

- **Melanoma Skin Cancer**
  - The incidence of melanoma skin cancer in the US is increasing, but the death rate due to melanoma is declining
    - From 2002 to 2006, the incidence of melanoma increased at a rate of 33% for men and 23% for women
    - Melanoma is increasing more rapidly than any other malignancy except lung cancer in women
    - Conversely, there have been recent declines in mortality for melanoma
    - From 2009 to 2013, the death rate for melanoma was stable, but from 2014 to 2018, the mortality due to melanoma declined 5.7% annually
  - In the US, it is estimated that there will be 106,110 new cases of melanoma diagnosed in 2021, and there will be an estimated 7,180 deaths due to melanoma
    - The median age at diagnosis is 65 years
    - Risk factors for the development of melanoma include both genetic factors (skin type, inherited germline mutations) and environmental factors (excess sun exposure, UV-based artificial tanning)
    - Despite the relationship to UV exposure, melanoma can also occur in areas of the body without substantial sun exposure and can occur in any ethnic group
  - There are also noncutaneous forms of melanoma, arising from melanocytes present in mucosal membranes or the uveal tract of the eye
    - The treatment of noncutaneous melanoma may differ from that of cutaneous melanoma, and treatment should be individualized for these patients

Oncology, Oral- Skin

- ONCOLOGY AGENTS : BRAF KINASE INHIBITORS – ORAL
  - Braftovi
  - **Tafinlar**
  - Zelboraf

- ONCOLOGY AGENTS : HEDGEHOG PATHWAY INHIBITORS – ORAL
  - Erivedge
  - Odomzo

- ONCOLOGY AGENTS : MEK INHIBITORS – ORAL
  - **Cotellic**
  - **Mekinist**
  - Mektovi

Oncology, Oral- Renal Cell Carcinoma

- **dabrafenib (Tafinlar)**
  - **March 2023: FDA approved in combination with trametinib (Mekinist) for treatment of pediatric patients ≥ 1 year of age with low-grade glioma (LGG) with a BRAF V600E mutation who require systemic therapy. Presence of BRAF V600E mutation in tumor specimens must be confirmed prior to treatment. An FDA-approved test for detection of this mutation in LGG is not currently available**
  - **Indications**
    - The treatment of patients with unresectable or metastatic melanoma with BRAF V600E or V600K mutations as detected by an FDA-approved test
    - The adjuvant treatment of patients with melanoma with BRAF V600E or V600K mutations, as detected by an FDA-approved test, and involvement of lymph node(s), following complete resection
    - The treatment of patients with metastatic non-small cell lung cancer (NSCLC) with BRAF V600E mutation as detected by an FDA-approved test
    - The treatment of patients with locally advanced or metastatic anaplastic thyroid cancer (ATC) with BRAF V600E mutation and with no satisfactory locoregional treatment options
    - The treatment of adult and pediatric patients 6 years of age and older with unresectable or metastatic solid tumors with BRAF V600E mutation who have progressed following prior treatment and have no satisfactory alternative treatment options. This indication is approved under accelerated approval based on overall response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s)
    - **The treatment of pediatric patients 1 year of age and older with low-grad glioma (LGG) with a BRAF V600E mutation who require systemic therapy**
  - **Dosage**
    - **The recommended dosage in adult patients is 150 mg orally twice daily**
    - **The recommended dosage in pediatric patients is based on body weight**
  - **Availability**
    - 50 mg and 75 mg capsules
    - **10 mg tablets for oral suspension**

Oncology, Oral- Renal Cell Carcinoma

- **cobimetinib (Cotellic)**
  - **November 2022: FDA approved a new indication for adults with histiocytic neoplasms as monotherapy**
  - **Indications**
    - For the treatment of adult patients with unresectable or metastatic melanoma with a BRAF V600E or V600K mutation, in combination with vemurafenib
    - **As a single agent for the treatment of adult patients with histiocytic neoplasms**
  - **Warning**
    - New primary malignancies, cutaneous and non-cutaneous: Monitor patients for new malignancies prior to initiation of therapy, while on therapy, and for up to 6 months following the last dose
    - Hemorrhage: Major hemorrhagic events can occur. Monitor for signs and symptoms of bleeding
    - Cardiomyopathy: The risk of cardiomyopathy is increased in patients receiving Cotellic with vemurafenib compared with vemurafenib as a single agent. The safety has not been established in patients with decreased left ventricular ejection fraction (LVEF). Evaluate LVEF before treatment, after one month of treatment, then every 3 months thereafter during treatment with Cotellic
  - **Dosage**
    - **Confirm the presence of BRAF V600E or V600K mutation in tumor specimens prior to initiation of Cotellic with vemurafenib for patients with melanoma**
    - **The recommended dose is 60 mg orally once daily for the first 21 days of each 28-day cycle until disease progression or unacceptable toxicity**
  - **Availability**
    - Tablets: 20 mg

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Oncology, Oral – Retinoids

ONCOLOGY AGENTS : RETINOIDS - ORAL

Appendices

Stimulants and Related Agents - Disease State Description & Guidelines

- Treatment
  - While continuous positive airway pressure (CPAP) therapy has been shown to improve daytime sleepiness in patients with obstructive sleep apnea (OSA), the level of sleepiness does not always normalize
  - To address this residual daytime sleepiness, pharmacologic treatments may be beneficial in users of CPAP
  - Modafinil (Provigil), armodafinil (Nuvigil), and solriamfetol (Sunosi) are FDA-approved for excessive daytime sleepiness associated with OSAHS. Modafinil and armodafinil are also indicated for sleep problems resulting from circadian rhythm disruption (e.g., SWSD)
  - Modafinil, armodafinil, pitolisant (Wakix), and solriamfetol, along with central nervous system (CNS) stimulants, such as dextroamphetamine (Dexedrine, Procentra, Zenzedi), methylphenidate (Methylin, Ritalin, Metadate ER), mixed amphetamine salts (Adderall), and amphetamine sulfate tablet (Evekeo), are used for narcolepsy
  - The potential for adverse cardiovascular events with CNS stimulant use may be of concern, especially in this overall high-risk patient population
  - Due to their lack of sympathomimetic activity, modafinil and armodafinil are relatively free of adverse cardiovascular effects

Stimulants and Related Agents - Guidelines

- American Academy of Pediatrics (AAP), 2011
  - The primary care clinician should initiate an evaluation for ADHD for any child 4 through 18 years of age who presents with academic or behavioral problems and symptoms of inattention, hyperactivity, or impulsivity
  - The treatment of patients with ADHD should maximize function to improve relationships and performance at school, decrease disruptive behaviors, promote safety, increase independence, and improve self-esteem
  - Treatment
    - Recommends parent- and/or teacher-administered behavior therapy as first-line treatment for children 4 to 5 years of age
    - 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
    - For children 6 to 11 years of age, the evidence is particularly strong for stimulant medication use and sufficient, but less strong evidence, for atomoxetine, extended-release guanfacine, and extended-release clonidine; however, medication therapy in addition to behavioral therapy is recommended
    - For patients 12 to 18 years of age, the AAP recommends FDA-approved medications, with the adolescent's assent, and behavior therapy as treatment for ADHD, preferably both American Academy of Pediatrics
    - Studies have shown that 70% to 75% of patients respond to the first stimulant medication on which they are started
      - Response increases to 90% to 95% when a second stimulant is tried
      - Treatment failures with stimulants are often due to improper doses rather than ineffectiveness of the medication
      - It may take 1 to 3 months to adequately establish the best dose and formulation for an individual patient
      - The AAP recommends that, if a trial with 1 drug compound group is ineffective or poorly tolerated, a trial of a medication from a different drug group should be used

Stimulants and Related Agents - Guidelines

- The Medical Letter, 2011
  - Suggests that school-age children begin with an oral stimulant, noting that none of the agents have shown to be more effective than another
  - They indicate that short-acting stimulants may be useful in small children to demonstrate effectiveness or in instances where there is not an appropriately low dose of a long-acting agent
  - The methylphenidate patch (Daytrana) is recommended for use when oral administration is problematic
  - Atomoxetine (Strattera), a non-stimulant agent, is recommended if there are objections to using a controlled substance, if stimulant-induced weight loss is problematic, or for patients with anxiety, mood, tic, or substance abuse disorders
  - Extended-release formulations of guanfacine or clonidine may be helpful when used concurrently with a stimulant in patients who cannot tolerate usual doses of the stimulant, particularly those with tics
  - Mixing short- and long-acting stimulants can be helpful to achieve an early stimulant effect for early-morning school classes or for reducing rebound irritability or overactivity toward the end of the day, especially when studying in the evening

- AACAP Guidelines
  - The American Academy of Child and Adolescent Psychiatry practice parameters for ADHD are now categorized as historical and can no longer be assumed to reflect current knowledge, as they have not been updated in over 5 years
  - AACAP clinical practice guidelines for ADHD are in development

Ophthalmic, Glaucoma Agents – Guidelines

- American Academy of Ophthalmology, 2018
  - The goal of treatment is to maintain the IOP in a range at which loss of visual field is unlikely to significantly affect a patient's health related quality of life over their lifetime
  - An initial target pressure is at least 25% lower than pretreatment IOP
    - However, target pressure is an estimate and should be individualized based on disease course; lower IOP targets are reasonable in patients with more severe optic nerve damage
  - Medical therapy is the most common initial intervention to lower IOP
    - Medication classes used in the management of glaucoma include beta-blockers, miotics, sympathomimetics, topical and oral carbonic anhydrase inhibitors, and prostaglandin F2α analogs
    - Monotherapy or combination therapy may be used to treat glaucoma and delay the need for surgery and prevent functional vision loss

- American Academy of Ophthalmology, 2020
  - Preferred practice patterns, prostaglandin analogs are the most frequently prescribed eye drops to lower IOP due to their efficacy, safety profile, and once-daily regimen
  - Sufficient management of glaucoma is dependent on a high level of adherence to therapy
  - Data has suggested the addition of a second medication can lead to reduced adherence; therefore, fixed dose combinations may potentially increase adherence and decrease exposure to preservatives
  - Although fixed dose combinations are not usually recommended as initial therapy, a fixed dose combination agent may be warranted in patients requiring a greater IOP reduction than available with a single agent

Guidelines - Oncology, Oral- Breast

- **Endocrine therapy for HR-positive disease**
  - According to the NCCN V2.2022 guidelines, endocrine therapy should be considered for nearly all patients with HR-positive disease, regardless of menopausal status, age, or HER2 status of the tumor, with the exception of patients with tumors ≤ 0.5 centimeters (cm) where adjuvant endocrine therapy is a category 2B rating
  - For patients recommended to receive both adjuvant endocrine therapy and adjuvant chemotherapy, these therapies should be given sequentially with endocrine therapy following chemotherapy
  - The NCCN guidelines regarding premenopausal women with HR-positive disease recommend tamoxifen for 5 years, with or without ovarian suppression or ablation or the use of an AI for 5 years plus ovarian suppression or ablation (both category 1)
    - After the initial 5 years of therapy, women who are still premenopausal may consider tamoxifen for an additional 5 years to complete 10 years or consider no further adjuvant endocrine therapy (both category 2A)
    - Women who subsequently became postmenopausal after the initial 5 years of adjuvant endocrine therapy may be treated with an AI for an additional 5 years (category 1) or may continue tamoxifen for an additional 5 years to complete 10 years of adjuvant therapy (category 2A)
    - The NCCN guidelines state that the 3 selective AIs, anastrozole, letrozole, and exemestane, have shown similar anti-tumor efficacy and toxicity profiles in randomized studies in the adjuvant and neoadjuvant settings and that the optimal duration of treatment with AIs in adjuvant setting is uncertain

Guidelines - Oncology, Oral- Breast

- **Targeted therapy for HER2-positive disease**
  - The 2020 ASCO guideline regarding optimal adjuvant chemotherapy and targeted therapy for early breast cancer gives a moderate rating of approval for the use of extended adjuvant therapy with neratinib following trastuzumab in patients with early-stage HER2-positive breast cancer
  - ASCO states they preferentially favor the use of neratinib in patients with HR-positive and node-positive disease. ASCO further states that neratinib causes substantial diarrhea and diarrheal prophylaxis must be used; patients who begin neratinib within 1 year of trastuzumab completion appear to derive the greatest benefit; and, at a median follow up of 5.2 years, no overall survival (OS) benefit has been observed for the use of extended adjuvant neratinib
  - Likewise, the NCCN guidelines state extended adjuvant neratinib may be considered following adjuvant trastuzumab-containing therapy in HR-positive, HER-2 positive, node positive patients with a perceived high risk of recurrence