Magellan Rx MANAGEMENT℠

Magellan Medicaid Administration

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Agenda Topics

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

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Antipsychotics, 2nd Generation

Overview of Disease State - Antipsychotics

Autism

- Autism spectrum disorder (ASD) is 1 of the most common development disabilities in children in the US
- Overall estimates of prevalence vary widely, but most recently was approximated at 16.8 per 1,000 children aged 8 years
- The Centers for Disease Control and Prevention (CDC) reported a recent rise in autism over the past few decades
- Two key criteria for the diagnosis of autistic disorder in the DSM-5 include
  - Impairments in social communication (verbal and nonverbal) and social interaction
  - A restrictive, repetitive range of interests, activities, and behavior

- American Academy of Child, 2014; Adolescent Psychiatry & American Academy of Pediatrics, 2016
  - Many medications that have been used for the treatment of autism are not indicated for the disorder; however, oral formulations of aripiprazole (Abilify) and risperidone (Risperdal) are FDA-approved for the treatment of irritability associated with autism in children
  - The AACAP recommends pharmacotherapy only when there is a specific symptom(s) targeted, but they do not specify the use of 1 antipsychotic agent over another
  - Similarly, guidelines from the American Academy of Pediatrics (AAP) have been published and do not specify the use of 1 antipsychotic agent over another
  - The AAP states that given the risks and benefits of atypical antipsychotics (e.g., aripiprazole, risperidone), these agents should only be used to treat severe irritability and problem behavior (I/PB) in ASD only in the following situations:
    - (1) Safety is an issue
    - (2) The behaviors interfere severely with current functioning (e.g., a change in school or residential placement would be necessary otherwise)
    - (3) Other interventions have failed or resulted in incomplete improvement
    - (4) Behavior is unrelated to psychosocial stressors, communication difficulties, underlying medical or psychiatric conditions, or environmental factors
    - (5) Lower-risk interventions cannot be implemented

Overview of Disease State - Antipsychotics

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

- 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

Overview of Disease State - Antipsychotics

Depression

- National epidemiological data among adults reported that the prevalence of 12-month and lifetime major depressive disorder (MDD), based on (DSM-5) criteria, is approximately 17.3 million American adults or 7.1% of the United States (US) population
- The US Preventive Services Task Force (USPSTF) recommends screening for MDD in adolescents ages 12 years and older and in adults
- This should be supplemented with precautions to ensure accurate diagnosis as well as appropriate treatment and follow-up
- The evidence for screening in patients younger than 12 years is insufficient to make a recommendation

- American Psychiatric Association (APA), 2010
  - For patients who exhibit psychotic symptoms during an episode of MDD, treatment should include a combination of antipsychotic and antidepressant medications or electroconvulsive therapy (ECT)
  - SGA medications may increase the rates of response or remission of depressive symptoms in patients who typically have not responded to more than 2 antidepressants, even when psychotic symptoms are not present
  - Generally, in clinical practice, lower doses are used for antidepressant augmentation than for treatment of psychosis
  - The APA does not consider these guidelines current based on publication date, but new updates or revisions have not been published

- American College of Physicians (ACP), 2016
  - After a review of the literature, they found that cognitive behavioral therapy (CBT) and second generation antidepressants are similarly effective and have similar discontinuation rates
  - ACP recommends treatment with either CBT or second generation antidepressants for MDD after discussing treatment effects, adverse effects, preferences, and accessibility with the patient
  - No clinical conclusions were made regarding the efficacy of SGAs

Overview of Disease State - Antipsychotics

Parkinson's Disease

- There is an estimated 1 million people living with PD in the US, with about 60,000 new cases diagnosed each year
- Parkinson's disease (PD) is a progressive, neurodegenerative disorder with cardinal motor features of tremor, bradykinesia, and rigidity
- ~20% to 30% of patients with PD experience hallucinations and up to 8% experience delusions in advanced stages of the disease
- Atypical antipsychotics have been used to treat hallucination and delusions associated with PD psychosis; however, in patients with only mild hallucinations, antipsychotic treatment may not be necessary

- American Academy of Neurology (AAN), 2006
  - In their 2006 guidelines, AAN recommends that clinicians consider clozapine for patients with PD and psychosis (Level B); the absolute neutrophil count must be monitored since clozapine can cause fatal agranulocytosis
  - Also, quetiapine does not exacerbate motor symptoms of PD and may be considered for patients with PD and psychosis (Level C)
  - Due to a better side effect profile, many clinicians may consider quetiapine as first-choice
  - Olanzapine and risperidone should not be used due to the potential for worsening motor function. Pimavanserin (Nuplazid) was not approved at the time of guideline development, but it is the only drug FDA-approved for the treatment of PD psychosis

Overview of Disease State - Antipsychotics

- American Psychiatric Assocation, 2016
  - The APA published practice guidelines on the use of antipsychotics to treat agitation or psychosis in patients with dementia
  - These guidelines do not specifically address the role of Nuplazid, but they do note that extrapyramidal side effects of other antipsychotic medications and the potential for cognitive worsening may be greater in individuals with Parkinson's disease dementia compared to other types of dementia

- Movement Disorders Society, 2019
  - An evidence-based review published in 2019 on behalf of the Movement Disorders Society found Nuplazid to be efficacious and to have an acceptable risk without requiring specialized monitoring
    - Thus, the researchers concluded that its use for psychosis in PD is clinically useful, but they also state that there is a lack of safety data regarding durability beyond 6 weeks
  - Notably, they also weigh in on other agents in this class that are not indicated for PD psychosis, stating that olanzapine is not clinically useful (not efficacious), quetiapine is possibly useful (limited evidence), and clozapine is also useful but requires specialized monitoring
  - They also emphasize that all antipsychotics should be used with great caution in demented patients with psychosis due to the risk of adverse effects (e.g., falls, impaired cognition, pneumonia, cardiovascular effects, stroke, and death)

Overview of Disease State - Antipsychotics

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

- American Psychiatric Association (APA), 2004
  - Goals of treatment are to stabilize the patient and reduce or eliminate the symptoms, improve quality of life and adaptive functioning, and reduce the likelihood of relapse
  - Antipsychotics are the standard drugs used in patients with schizophrenia to achieve these goals
  - This guideline recommends a second generation antipsychotic (SGA) as first-line therapy due to the decreased risk of extrapyramidal symptoms (EPS) and tardive dyskinesia (TD), with first generation antipsychotics (FGA) suggested as appropriate first-line options for some patients
  - The 2009 Guideline Watch from the APA modifies this recommendation to state that FGAs may be equally effective as second generation agents
  - This statement is based on studies that have been published since 2002
  - Notably, as these guidelines are more than 5 years old, the APA does not consider them current; however, they have not published updates or revisions
- 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**

Overview of Disease State - Antipsychotics

Tourette's Disorder

- The prevalence of Tourette's disorder is unknown, but observational studies have suggested a prevalence of 1% in school-aged children
- Tourette's disorder is a genetic tic disorder characterized by motor and vocal tics
- Generally, individuals have repetitive, stereotyped movements of vocalizations (e.g., sniffing, muscle tension, blinking)
  - DSM-5 criteria for Tourette's disorder state multiple motor and at least 1 vocal tics are present during the illness (not necessarily simultaneously) and have been present for ≥ 1 year, although they may wax and wane in frequency
- Onset of these symptoms must occur prior to 18 years of age to be considered Tourette's disorder
  - Peak tic severity typically occurs between the ages of 10 and 12 years
- Tics usually improve during adolescence, with 18% of those older than 16 years experiencing no tics and 60% having minimal or mild tics 6 years after initial examination

- American Academy of Neurology, 2019
  - No evidence exists demonstrating that treatment is more effective the earlier it is started and watchful waiting is reasonable, especially in those without tic-related functional impairment
  - Comprehensive behavioral intervention for tics (CBIT) may be considered as initial therapy in patients who are motivated to attempt treatment
  - Patients should be assessed for comorbid conditions such as ADHD, OCD, anxiety disorders, oppositional defiant disorder, and mood disorders
  - Alpha-2 adrenergic agonists (e.g., clonidine, guanfacine) may reduce tic severity, particularly in patients with ADHD
  - Regarding other specific pharmacologic agents
    - Haloperidol, risperidone, aripiprazole, and Botox are probably more likely than placebo to reduce tic severity
    - Pimozide, ziprasidone, topiramate, and metoclopramide are possibly more likely than placebo to reduce tic severity
    - Overall, however, there is insufficient evidence to determine the relative efficacy of these drugs
  - Notably, a higher risk of drug-induced movement disorders is associated with haloperidol, pimozide, and risperidone and with long-term use of metoclopramide
  - Patients with severe Tourette syndrome resistant to medical and behavioral therapy may benefit from deep brain stimulation (DBS)

Antipsychotics – Indications

Drug	Generic	Other Indications	Schizophrenia	Bipolar Disorder			
				Acute Manic Episodes	Depressive Episodes	Acute Mixed Episodes	Maintenance
Second Generation Antipsychotics – Oral							
aripiprazole (Abilify)	**X**	Major depressive disorder (adjunct); Irritability associated with autistic disorder (ages 6 to 17 years); Tourette's disorder (ages 6 to 18 years)	**X** (ages ≥ 13 years)	**X** (ages ≥ 10 years for acute treatment as monotherapy and in combination with lithium or valproate)	**--**	**X** (ages ≥ 10 years for acute treatment as monotherapy and in combination with lithium or valproate)	**X** (monotherapy and in combination with lithium or valproate for ages ≥ 10 years)
aripiprazole (with sensor) (Abilify Mycite)	**--**	Major depressive disorder (adjunct)	**X**	**X** (acute treatment as monotherapy and in combination with lithium or valproate)	**--**	**X** (acute treatment as monotherapy and in combination with lithium or valproate)	**X** (monotherapy and in combination with lithium or valproate)

Antipsychotics – Indications

Drug	Generic	Other Indications	Schizophrenia	Bipolar Disorder			
				Acute Manic Episodes	Depressive Episodes	Acute Mixed Episodes	Maintenance
Second Generation Antipsychotics – Oral (*continued*)							
asenapine (Saphris)	--	--	X	X (ages ≥ 10 years for acute treatment as monotherapy; adults in combination with lithium or valproate)	--	X (ages ≥ 10 years for acute treatment as monotherapy; adults in combination with lithium or valproate)	X (monotherapy; adults only)
brexpiprazole (Rexulti)	--	Major depressive disorder (adjunct)	X	--	--	--	--
cariprazine (Vraylar)	--	--	X	X (acute treatment)	--	X (acute treatment)	--
clozapine (Clozaril)	X	--	X (treatment-resistant schizophrenia; reducing suicidal behavior in schizophrenia or schizoaffective disorder)	--	--	--	--
clozapine (Fazaclo)	X						
clozapine (Versacloz)	--						
iloperidone (Fanapt)	--	--	X	--	--	--	--
lurasidone (Latuda)	--	--	X (ages ≥ 13 years)	--	X (ages ≥ 10 years as monotherapy and in adults in combination with lithium or valproate)	--	--

Antipsychotics – Indications

Drug	Generic	Other Indications	Schizophrenia	Bipolar Disorder			
				Acute Manic Episodes	Depressive Episodes	Acute Mixed Episodes	Maintenance
Second Generation Antipsychotics – Oral (*continued*)							
olanzapine (Zyprexa)	X	Treatment-resistant depression (in combination with fluoxetine)	X (ages ≥ 13 years; second-line in adolescents due to metabolic effects)	X (ages ≥ 13 years as monotherapy and in combination with lithium or valproate; second-line in adolescents due to metabolic effects)	X (ages ≥ 10 years; in combination with fluoxetine)	X (ages ≥ 13 years as monotherapy and in combination with lithium or valproate; second-line in adolescents due to metabolic effects)	X (ages ≥ 13 years)
olanzapine/ fluoxetine (Symbyax)	X	Treatment-resistant depression	--	--	X (ages ≥ 10 years for acute episodes)	--	--
paliperidone ER (Invega)	X	Schizoaffective disorder (monotherapy or adjunct with mood stabilizers and/or antidepressants)	X (ages ≥ 12 years)	--	--	--	--
pimavanserin (Nuplazid)	--	Hallucinations and delusions associated with Parkinson's disease (PD) psychosis	--	--	--	--	--
quetiapine (Seroquel)	X	--	X (ages ≥ 13 years)	X (ages ≥ 10 years as monotherapy; adults in combination with lithium or valproate)	X	--	X (in combination with lithium or divalproex)

Antipsychotics – Indications

Drug	Generic	Other Indications	Schizophrenia	Bipolar Disorder			
				Acute Manic Episodes	Depressive Episodes	Acute Mixed Episodes	Maintenance
Second Generation Antipsychotics – Oral (*continued*)							
quetiapine ER (Seroquel XR)	X	Major depressive disorder (adjunct)	X (ages ≥ 13 years)	X (ages ≥ 10 years as monotherapy; adults in combination with lithium or valproate)	X	X (ages ≥ 10 years as monotherapy; adults in combination with lithium or valproate)	X (in combination with lithium or divalproex)
risperidone (Risperdal)	X	Irritability associated with autistic disorder (ages 5-17 years)	X (ages ≥ 13years)	X (ages ≥ 10 years as monotherapy; adults in combination with lithium or valproate)	--	X (ages ≥ 10 years as monotherapy; adults in combination with lithium or valproate)	--
ziprasidone (Geodon)	X	--	X	X (acute episodes)	--	X (acute episodes)	X (in combination with lithium or divalproex)

Antipsychotics – Indications

Drug	Generic	Other Indications	Schizophrenia	Bipolar Disorder
Second Generation Antipsychotics – Short Acting Injectable				
olanzapine (Zyprexa)	**X**	Acute agitation associated with schizophrenia or bipolar mania	**--**	**--**
ziprasidone (Geodon)	**--**	**--**	X (acute agitation)	**--**
aripiprazole ER (Abilify Maintena)	**--**	**--**	**X**	X (maintenance treatment as monotherapy)
aripiprazole lauroxil ER (Aristada)	**--**	**--**	**X**	**--**
aripiprazole lauroxil ER (Aristada Initio)	**--**	**--**	**X** (for initial dose or select missed doses only)	**--**
olanzapine (Zyprexa Relprevv)	**--**	**--**	**X**	**--**
paliperidone palmitate (Invega Sustenna)	**--**	Schizoaffective disorder (monotherapy and as an adjunct to mood stabilizers or antidepressants)	**X**	**--**
paliperidone palmitate (Invega Trinza)	**--**	**--**	**X** (treatment in patients after they have been adequately treated with Invega Sustenna for ≥ 4 months)	**--**
risperidone ER microspheres (Risperdal Consta)	**--**	**--**	**X**	**X** (maintenance treatment as monotherapy or in combination with lithium or valproate)
risperidone ER suspension‖ (Perseris)	**--**	**--**	**X**	**--**

Antipsychotics – New Medication

- **Nuplazid (pimavanserin)**
  - **Indication:**
    - **Indicated for the treatment of hallucinations and delusions associated with Parkinson's disease psychosis**
  - **Warning & Precautions:**
    - **QT Interval Prolongation: Increases in QT interval; avoid use with drugs that also increase the QT interval and in patients with risk factors for prolonged QT interval**
    - **Increased Mortality in Elderly Patients with Dementia-Related Psychosis**
    - **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 unrelated to the hallucinations and delusions associated with Parkinson's disease psychosis**
  - **Dosage:**
    - **Recommended dose is 34 mg taken orally once daily, without titration**
    - **Can be taken with or without food**
  - **Availability:**
    - **Capsules: 34 mg**
    - **Tablets: 10 mg**

Antipsychotics – New Medication

- **Vraylar (cariprazine)**
  - **Indication:**
    - **An atypical antipsychotic indicated for the:**
      - **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 adult**
  - **Warning & Precautions:**
    - **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**
    - **Antidepressants increased the risk of suicidal thoughts and behaviors in pediatric and young adult patients**
    - **Closely monitor all antidepressant treated patients for clinical worsening and emergence of suicidal thoughts and behaviors**
  - **Dosage:**
    - **Administer once daily with or without food**
    - **Schizophrenia: 1.5 mg daily (starting dose); 1.5 mg to 6 mg daily (recommended dose)**
    - **Bipolar Mania: 1.5 mg daily (starting dose); 3 mg to 6 mg daily (recommended dose)**
    - **Bipolar Depression: 1.5 mg daily (starting dose); 1.5 mg or 3 mg daily (recommended dose)**
    - **Schizophrenia and Bipolar Mania: Dosages above 6 mg daily do not confer significant benefit but increase the risk of dose-related adverse reactions**
  - **Availability:**
    - **Capsules: 1.5 mg, 3 mg, 4.5 mg, and 6 mg**

Antipsychotics

Black Box Warnings

- All antipsychotics, including pimavanserin (Nuplazid), have a boxed warning regarding an increased incidence of mortality when these agents are used in elderly patients with dementia-related psychosis
- Aripiprazole (Abilify, Abilify Mycite), lurasidone (Latuda), olanzapine/fluoxetine (Symbyax), and quetiapine (Seroquel, Seroquel XR) have the same boxed warning as the antidepressants in regards to an increased risk of suicidality in children, adolescents, and young adults
- Clozapine (Clozaril, Fazaclo, Versacloz) has several additional boxed warnings:
  - Due to a significant risk of severe neutropenia (absolute neutrophil count < 500/µL), which may increase the risk of serious and potentially fatal infections, clozapine is only available through the Clozapine Risk Evaluation and Mitigation Strategy (REMS) Program
  - Seizures are associated with the use of clozapine (cumulative incidence at 1 year of 5%); this is a dose-related effect
    - Caution must be used when administering clozapine to patients with a history of seizures or predisposition to seizures
    - Patients must also be warned to avoid engaging in activities where a loss of consciousness may cause harm to themselves or others
  - Myocarditis occurs with clozapine at a rate of 5 cases per 100,000 patient years; over half of these cases were fatal
    - Clozapine also carries warnings for cardiomyopathy and mitral valve incompetence
- Orthostatic hypotension with rare collapse (1 case per 3,000 patients) and respiratory and/or cardiac arrest occur at a higher rate in patients receiving clozapine, especially during dose escalation in the initial titration phase
- Loxapine inhalation powder (Adasuve) has a boxed warning cautioning of bronchospasms that can potentially lead to respiratory distress and respiratory arrest
  - Healthcare facilities administering loxapine inhalation powder must have access to short-acting bronchodilators for immediate treatment of bronchospasms
- Olanzapine (Zyprexa Relprevv) has a boxed warning stating that patients are at risk for Post-injection Delirium Sedation Syndrome (PDSS)
  - This syndrome may result in severe sedation, including coma, and/or delirium after each injection
  - Patients should be observed for at least 3 hours in a healthcare facility with access to emergency response services following administration
- Thioridazine has a boxed warning regarding its tendency to prolong the QTc interval in a dose-related manner

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Antimigraine Agents (CGRP Agents)

Disease State Description
Antimigraine Agents

- **Migraine**
  - Accounts for 10% to 20% of all headaches in adults and affects over 39 million men, women, and children in the United States
  - Headache is one of the most common complaints by patients when presenting to a physician
    - 64% of physician-diagnosed patients who experience migraines and 41% of undiagnosed migraine sufferers reported severe impairment or the need for bed rest due to their migraine symptoms
    - In addition, 18% of women, 6% of men, and 10% of children experience migraine, an epidemiologic profile that has remained stable over many years
  - Approximately 85% of patients with migraine headaches suffer less than 3 to 4 attacks per month
    - The median frequency of migraine attacks among migraine sufferers is 1.5 per month
  - Migraine headache must be differentiated from tension-type headache
    - Key criteria for the diagnosis of migraine headache includes an episodic headache lasting from 4 to 72 hours with at least 2 of the following symptoms: unilateral pain, throbbing, aggravated by routine physical activity, pain of moderate to severe intensity
    - During the headache at least 1 of the following are present: nausea and/or vomiting, or photophobia and phonophobia

Migraine Research Foundation, 2018

Disease State Description
Antimigraine Agents

- **Migraine**
  - A complex neurological condition that can involve debilitating headache and sensory changes
  - During a migraine attack neurologic changes occur in the cortex, brainstem, hypothalamus, thalamus, as well as, peripheral and central portions of the trigeminovascular system
  - Migraine attacks are usually episodic, occurring < 15 days per month, but some migraine sufferers experience chronic daily headaches ≥ 15 days per month, often with migrainous features
  - Key features for the diagnosis of migraine headache includes an episodic headache lasting 4 to 72 hours with at least 2 of the following symptoms:
    - Unilateral pain
    - Throbbing
    - Aggravated by routine physical activity
    - Pain of moderate to severe intensity
  - During the migraine at least 1 of the following are present: nausea and/or vomiting, or photophobia and/or phonophobia

Disease State Description - Antimigraine Agents

- **Cluster Headache (CH)**
  - A severe, primary headache disorder characterized by extreme pain on one side of the head and autonomic symptoms (e.g., nasal congestion, lacrimation)
  - CH periods can persist for weeks to months with daily or more frequent attacks of 15 to 180 minutes in duration
  - The estimated lifetime prevalence of CH is more than one in 1,000. CH can be either episodic or chronic in nature with episodic CH being the predominant form
  - Individuals with episodic CH experience periods of attack followed by periods of remission, whereas individuals with chronic CH have minimal to no periods of remission between headache attacks

American Headache Society, 2016

Antimigraine – Indications, Dosing & Availability

Drug	Generic	Indication(s)
erenumab-aooe (Aimovig)	---	• Preventive treatment of migraine in adults
fremanezumab-vfrm (Ajovy)	---	• Preventive treatment of migraine in adults
galcanezumab-gnlm (Emgality)	---	• Preventive treatment of migraine in adults • Treatment of episodic cluster headache in adults

Drug	Indication	Dosage	Availability
erenumab-aooe (Aimovig)	• Preventive treatment of migraine	70 mg SC once monthly; some patients may benefit 140 mg SC once monthly	70 mg/1 mL and 140 mg/1 mL single-dose prefilled SureClick autoinjector (cartons contain one or two 70 mg/1 mL autoinjectors or one 140 mg/1 mL autoinjector)
fremanezumab-vfrm (Ajovy)	• Preventive treatment of migraine	225 mg once SC monthly or 675 mg every 3 months (administer as 3 consecutive 225 mg injections) When switching dosage options, administer the first dose of the new regimen on the next scheduled date of administration	225 mg/1.5 mL single-dose prefilled syringe (carton contains 1 syringe)
galcanezumab-gnlm (Emgality)	• Preventive treatment of migraine	240 mg SC (administered as 2 consecutive 120 mg injections) once as a loading dose, followed by 120 mg SC once monthly	120 mg/1 mL single-dose prefilled syringe and single-dose prefilled pen (carton contains 1 prefilled syringe or pen)
	• Treatment of episodic cluster headache	300 mg SC (administered as 3 consecutive 100 mg SC injections) at the onset of symptoms, followed by 300 mg SC monthly through the end of the cluster period	100 mg/1 mL single-dose prefilled syringe (carton contains 3 prefilled syringes)

Antimigraine Agents – Guidelines

- In 2018, the FDA approved the first calcitonin gene-related peptide (CGRP) inhibitors, erenumab-aooe (Aimovig), fremanezumab-vfrm (Ajovy), and galcanezumab-gnlm (Emgality), for preventative treatment of migraines in adults

- <u>The American Headache Society (AHS), 2019</u>
  - Released a position statement on integrating new migraine treatments into clinical practice
  - Unlike oral prophylaxis agents, the CGRP inhibitors do not require slow dose escalation, have a faster onset of therapeutic benefit, and have favorable tolerability profiles
  - The AHS recommends initiating CGRP inhibitors for migraine prophylaxis in patients ≥ 18 years of age with the following:
    - Diagnosis of migraine (with or without aura) experiencing 4 to 7 monthly headache days with moderate disability and inability to tolerate or inadequate response to a 6-week trial of at least 2 oral prophylactic agents
    - Diagnosis of migraine (with or without aura) experiencing 8 to 14 monthly headache days and inability to tolerate or inadequate response to a 6-week trial of at least 2 oral prophylactic agents
    - Diagnosis of chronic migraine and either inability to tolerate or inadequate response to a 6-week trial of at least 2 oral prophylactic agents or at least 6 months of onabotulinumtoxinA treatment
  - According to the AHS response to CGRP inhibitor therapy should be assessed after 3 months (for monthly injections) or 6 months (for quarterly injections)
  - Therapy should only be continued if clinically meaningful treatment benefit can be documented
  - The statement also addresses non-pharmacologic therapy, including neuromodulation and biobehavioral therapies

Antimigraine Agents – Guidelines

- American Headache Society (AHS), 2016
  - Recommends sumatriptan subcutaneous (SC) at a dose of 6 mg, zolmitriptan nasal spray at a dose of 5 mg or 10 mg, and 100% oxygen at 6 to 12 L/minute for the acute treatment of episodic or chronic CH (Level A recommendation)
  - Pharmacological therapies considered to be probably effective (Level B) for episodic and chronic CH include sumatriptan nasal spray 20 mg as well as zolmitriptan oral at a 5 mg or 10 mg dose
  - Sphenopalatine ganglion stimulation is a potential nonpharmacological treatment option for patients with chronic CH who are not satisfied with current therapy (Level B); however, it is not routinely available in the US
  - Octreotide 100 mcg SC as well as lidocaine 10% nasal spray are considered to be possibly effective (Level C) for both episodic as well as chronic CH
  - As of the date of guideline publication, insufficient evidence (Level U) existed to support the use of dihydroergotamine nasal spray, somatostatin, or prednisone
  - In general, the strength of the recommendation for the treatment modality should be considered in conjunction with the potential safety profile, prescriber experience, patient-specific factors, and cost
  - Emgality is the first FDA-approved treatment for episodic CH that decreases the frequency of acute attacks
    - It was not available at the time of the AHS guideline development

Antimigraine Agents – Guidelines

- American Academy of Neurology (AAN) and American Headache Society (AHS), 2015
  - Non-opioid analgesia with a nonsteroidal anti-inflammatory drugs (NSAIDs), or combinations such as aspirin or acetaminophen plus caffeine, are recommended as first-line therapy for patients with mild to moderate migraine pain
  - Due to well-established efficacy, the triptans have become the drugs of choice for treating migraine attacks
    - Response rate to triptans is about 60%
    - Studies suggest that 38% to 50% of migraineurs are candidates for preventive therapy
  - Indications for preventive therapy include
    - ≥ 4 migraine attacks per month or ≥ 8 migraine days per month
    - Acute medication overuse
    - Debilitating migraine
  - Advise that antiepileptic drugs (divalproex sodium, sodium valproate, topiramate) and beta-blockers (metoprolol, propranolol, timolol) are established as effective in migraine prevention
  - Naratriptan, zolmitriptan, antidepressants (amitriptyline, venlafaxine), and beta-blockers (atenolol, nadolol) are probably effective in migraine prevention; but no triptan is approved for the prevention of migraines
  - All available triptans (almotriptan; eletriptan; frovatriptan; naratriptan; rizatriptan; sumatriptan oral, nasal, injectable, and transdermal; and zolmitriptan oral and nasal) are effective treatments
  - Dihydroergotamine (nasal, inhaler), acetaminophen, NSAIDs, select opioids, sumatriptan/naproxen, and acetaminophen/aspirin/caffeine were also rated as effective
  - No recommendation was offered regarding an advantage of 1 triptan over another
  - An update to this guideline is in progress

Antimigraine Agents – Guidelines

- American Academy of Neurology (AAN) and American Headache Society (AHS), 2019
  - Issued new guidelines on pharmacologic treatment for pediatric migraine prevention
  - Key recommendations include: counsel patients and caregivers on lifestyle modifications (sleep habits, tobacco use)
  - Advise patients and caregivers that most trials of preventive medications have failed to show any benefit over placebo in children, except for propranolol which may "possibly" result in a 50% reduction in headache frequency
    - Counsel patients/caregivers to treat an attack early for most benefit (first-line ibuprofen oral solution [10 mg/kg] in children and adolescents)
    - Counsel patients/caregivers about medication overuse
  - Sumatriptan/naproxen tablets and zolmitriptan nasal spray are options in adolescents
  - Offer antiemetics to treat substantial nausea and vomiting

Magellan Rx MANAGEMENT℠

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Antipsychotics, 1st Generation

Antipsychotics – Indications

Drug	Generic	Other Indications	Schizophrenia	Psychotic Disorders	Bipolar Disorder (acute manic episodes)
First Generation Antipsychotics – Oral					
amitriptyline/ perphenazine	--	Moderate to severe anxiety and/or agitation and depressed mood; depressed patients in whom anxiety and/or agitation are severe; depression and anxiety in association with chronic physical disease	--	--	--
chlorpromazine	X	Acute intermittent porphyria; intractable hiccups; presurgical apprehension and/or restlessness (ages ≥ 6 months); N/V (ages ≥ 6 months); tetanus (adjunct); severe behavioral problems in children (ages 1 to 12 years); short-term treatment of hyperactive children with accompanying conduct disorder (ages 1 to 12 years)	X	X	X
fluphenazine	X	--	--	X	--
haloperidol	X	Severe behavior problems in children with combative, explosive hyperexcitability following prior therapy failure (ages 3 to 12 years); short-term treatment of hyperactive children with accompanying conduct disorder following prior therapy failure (ages 3 to 12 years); tics and vocal utterances associated with Tourette's disorder (ages ≥ 3 years)	--	X (ages ≥ 3 years)	--
loxapine	X	--	X	--	--
molindone	--	--	X (ages ≥ 12 years)	--	--
perphenazine	X	N/V (ages ≥ 12 years)	X (ages ≥ 12 years)	--	--
pimozide (Orap)	X	Motor and phonic tics associated with Tourette's disorder (second-line; ages ≥ 2 years)	--	--	--

Antipsychotics – Indications

Drug	Generic	Other Indications	Schizophrenia	Psychotic Disorders	Bipolar Disorder (acute manic episodes)
First Generation Antipsychotics – Oral *(continued)*					
thioridazine	**X**	**--**	**X (second-line; pediatrics)**	**--**	**--**
thiothixene	**--**	**--**	**X (ages ≥ 12 years)**	**--**	**--**
trifluoperazine	**X**	Non-psychotic anxiety (second-line; up to 12 weeks)	**X (ages ≥ 6 years)**	**--**	**--**
First Generation Antipsychotics – Inhaled					
loxapine inhalation powder (Adasuve)	**--**	Acute agitation associated with bipolar I	**X (acute agitation associated with schizophrenia)**	**--**	**--**
First Generation Antipsychotics – Short Acting Injectable					
chlorpromazine hydrochloride	**X**	Acute intermittent porphyria; intractable hiccups; presurgical apprehension (ages ≥ 6 months); N/V (ages ≥ 6 months); tetanus (adjunct; ages ≥ 6 months); short-term treatment of hyperactivity in children with conduct disorder (ages 1 to 12 years); severe behavioral problems in children (ages 1 to 12 years)	**X**	**--**	X (mania)
fluphenazine hydrochloride	**X**	**--**	**--**	**X**	**--**
haloperidol lactate (Haldol)	**X**	Tics and vocal utterances of Tourette's disorder	**X**	**--**	**--**

Antipsychotics – Indications

Drug	Generic	Other Indications	Schizophrenia	Psychotic Disorders	Bipolar Disorder (acute manic episodes)
First Generation Antipsychotics – Long Acting Injectable					
fluphenazine decanoate	X	--	X	--	--
haloperidol decanoate (Haldol Decanoate)	X	--	X	--	--

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Antimanic Agents (Lithium Agents)

Overview of Disease State – Antimanic Agents

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
- Criterion used to diagnose a bipolar II disorder includes 1 or more depressive episodes nearly every day during the same 2-week period with at least 1 hypomanic episode lasting at least 4 days
  - The depressive episodes are marked by the appearance of 5 or more depressed symptoms, which include a depressed mood most of the day every day, diminished interest in activities and hobbies, significant weight change, insomnia or hypersomnia, psychomotor agitation or retardation nearly every day, fatigue, feeling of guilt or worthlessness, indecisiveness or inability to concentrate, and recurrent thoughts of death or suicide
- Hypomanic episodes are defined as a persistently elevated, expansive, or irritable mood with increased energy/activity and 3 or more other symptoms
  - These symptoms include inflated self-esteem, decreased need for sleep, pressured speech, distractibility, increase in goal-directed behavior, and excessive involvement with risky activities
  - The diagnosis of hypomania is very similar to mania, but the episodes do not result in significant impairment of functioning; they do not necessitate hospitalization and no psychotic symptoms are present

Overview of Disease State – Antimanic Agents

- 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 antidepressants in bipolar patients, misdiagnosed as having non-bipolar depression, can precipitate the first manic episode
  - The first-line treatment for a bipolar depressive disorder, includes treatment initiation with **lithium** or **lamotrigine**; antidepressant monotherapy is not recommended.
    - An alternative treatment option for more severe depressive episodes is the initiation of **lithium** with an **antidepressant**
    - If an acute depressive episode does not respond to the optimal dose of first-line medication treatment, then the addition of **lamotrigine**, **bupropion**, or **paroxetine** is recommended
    - Patients with bipolar depression experiencing psychotic features usually require adjunctive treatment with an antipsychotic
    - The 2005 Guideline Watch states that olanzapine/fluoxetine (**Symbyax**) and quetiapine (**Seroquel**) may also be effective for depressive episodes
  - 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 if dose optimization of the initial agent does not lead to a satisfactory response
    - Another option is to change antipsychotic agents and monitor the patient for response
  - 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

Overview of Disease State – Antimanic Agents

- American Psychiatric Association (APA), 2002
  - Following remission of an acute episode, patients may remain at particularly high risk of relapse for a period of up to 6 months
    - This phase of treatment is considered in the APA guideline as part of the maintenance phase
  - The medications with the best empirical evidence to support their use in maintenance treatment include **lithium** and **valproate**; possible alternatives include **lamotrigine**, **carbamazepine**, or **oxcarbazepine**
    - If 1 of these medications was used to achieve remission from the most recent depressive or manic episode, it generally should be continued
    - For patients treated with an antipsychotic medication during the preceding acute episode, the need for ongoing antipsychotic treatment should be reassessed
    - Varying levels of evidence exist for maintenance treatment of bipolar disorder
  - Again, as these guidelines are more than 5 years old, the APA does not consider them current; however, they have not published updates or revisions

Antimanic Agents (Lithium Agents) – Indications

Lithium Agents; Current Product Listing

LABEL NAME	MANUFACTURER	DRUG TYPE	PROVIDER SYNERGIES BRAND NAME ROUTE
LITHIUM CARBONATE 150 MG CAP	generic	GEN	LITHIUM CARBONATE CAPSULE (ORAL)
LITHIUM CARBONATE 300 MG CAP	generic	GEN	LITHIUM CARBONATE CAPSULE (ORAL)
LITHIUM CARBONATE 600 MG CAP	generic	GEN	LITHIUM CARBONATE CAPSULE (ORAL)
LITHIUM CARBONATE 300 MG TAB	generic	GEN	LITHIUM CARBONATE TABLET (ORAL)
LITHIUM 8 MEQ/5 ML SOLUTION	ROXANE/WEST-WAR	GEN	LITHIUM CITRATE (ORAL)
LITHIUM CARBONATE ER 300 MG TB	generic	GEN	LITHIUM ER (ORAL)
LITHIUM CARBONATE ER 450 MG TB	generic	GEN	LITHIUM ER (ORAL)

Antimanic Agents – New Medication

- **Equetro (carbamazepine)**
  - **Indication:**
    - **A mood stabilizer indicated for the treatment of acute manic or mixed episodes associated with bipolar I disorder**
    - Indicated for the treatment of the pain associated with trigeminal neuralgia
    - An anti-epileptic drug (AED) indicated for the treatment of partial seizures with complex symptomatology, generalized tonic-clonic seizures, and mixed seizures
  - **Black Box Warning:**
    - **Serious Dermatologic Reactions**
      - **Serious and sometimes fatal dermatologic reactions, including toxic epidermal necrolysis (TEN) and Stevens-Johnson Syndrome (SJS), have occurred**
      - **Patients of Asian ancestry have a 10-fold greater risk of TEN/SJS, compared to other populations**
      - **Discontinue EQUETRO if these reactions occur**
    - **Aplastic Anemia and Agranulocytosis**
      - **Aplastic anemia and agranulocytosis occurred with Equetro**
      - **Obtain complete pretreatment hematological testing**
      - **Consider discontinuing Equetro if significant bone marrow depression develops**
  - **Dosage:**
    - **See dosage for indications in TCR**
    - **When discontinuing treatment, reduce dose gradually; do not crush or chew capsules or beads**
    - **Swallow capsules whole or open capsules and sprinkle beads over food**
    - **Monitoring serum carbamazepine concentrations may be useful in dose selection and minimizing risk of toxicity**
  - **Availability:**
    - **Extended-Release Capsules: 100 mg, 200 mg, and 300 mg**

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Antimigraine Agents: Triptans & Others

Antimigraine, Triptans & Others – Indications

Drug	Generic	Indication(s)
almotriptan	**X**	• Acute treatment of migraine attacks with or without aura in adults and in adolescents 12 to 17 years of age whose attacks usually last 4 hours or more
eletriptan (Relpax)	**X**	• Acute treatment of migraine attacks with or without aura in adults
frovatriptan (Frova)	**X**	
naratriptan (Amerge)	**X**	
rizatriptan (Maxalt, Maxalt-MLT)	**X**	• Acute treatment of migraine attacks with or without aura in adults and in pediatric patients 6 to 17 years of age
sumatriptan (Imitrex)	**X**	• Acute treatment of migraine attacks with or without aura in adults (all formulations) • Injection: Acute treatment of cluster headache episodes in adults
sumatriptan (Onzetra Xsail)	**---**	• Acute treatment of migraine attacks with or without aura in adults
sumatriptan (Sumavel DosePro)	**---**	• Acute treatment of migraine attacks with or without aura in adults • Acute treatment of cluster headache episodes in adults
sumatriptan (Zembrace SymTouch)	**---**	• Acute treatment of migraine with or without aura in adults
sumatriptan/naproxen (Treximet)	**X**	• Acute treatment of migraine attacks with or without aura in those ≥ 12 years of age
sumatriptan; camphor/menthol (Migranow)	**---**	• Acute treatment of migraine attacks with or without aura in adults
zolmitriptan (Zomig, Zomig-ZMT)	**X**	• Acute treatment of migraine attacks with or without aura in adults

Antimigraine, Triptans & Others – Indications

Drugs	Generic	Indications	Availability
Erenumab-Aooe) Aimovig	---	- Preventative treatment of migraine in adults	- SC Injection: 70mg/mL solution in a single-dose prefilled SureClick autoinjector - SC Injection: 70 mg/mL solution in a single-dose prefilled syringe
Ergotamine Tartrate and Caffeine (Cafergot)	---	- Therapy to abort or prevent vascular headache (i.e. migraine, migraine variants, or so-called “histaminic cephalalgia”)	- Tablets (1 mg ergotamine tartrate and 100 mg caffeine)
Diclofenac Potassium (Cambia)	---	- Treat migraine attacks with or without aura in adults 18 years of age or older	- Individual oral packets each designed to deliver a 50 mg dose when mixed with 30-60 mL of water
Dihydroergotamine Mesylate	X	- Acute treatment of migraine headaches with or without aura - Acute treatment of cluster headache episodes	- 1 mL injections (IV, IM, or SC)
Dihydroergotamine Mesylate (Migranal)	X	- Acute treatment of migraine headaches with or without aura	- Nasal spray (0.5 mg) in 4 mg/mL spray
Ergomar (Ergotamine Tartrate)	---	- Therapy to abort or prevent vascular headache (i.e. migraine, migraine variants or a so-called “histaminic cephalalgia”)	- Sublingual Tablets (2 mg)
Isometheptene/ Caffeine/ APAP (Prodrin)	X	- Treatment of tension and vascular headaches	- Tablets (65mg/20mg/325mg)
Isometheptene/Dichloralphenazone /APAP (Midrin)	X	- Treatment of tension and vascular headaches	- Capsule (65 mg, 100 mg, 325mg)
Ergotamine Tartrate and Caffeine (Migergot)	X	- Therapy to abort or prevent vascular headache (i.e. migraine, migraine variants, or so-called “histaminic cephalalgia”)	- Rectal suppository (2mg/100mg)

Antimigraine, Triptans & Others – New Medication

- **Reyvow (lasmiditan)**
  - **October 11, 2019: FDA approved Reyvow, a serotonin (5-HT) 1F receptor agonist indicated for the acute treatment of migraine with or without aura in adults**
  - **Indication:**
    - **The acute treatment of migraine with or without aura in adults**
    - **Limitations of Use: not indicated for the preventive treatment of migraine**
    - **Contains lasmiditan (Controlled substance schedule to be determined after review by the Drug Enforcement Administration)**
  - **Warning & Precautions:**
    - **Driving Impairment: Advise patients not to drive or operate machinery until at least 8 hours after taking each dose**
    - **May cause CNS depression and should be used with caution if used in combination with alcohol or other CNS depressants**
    - **Reactions consistent with serotonin syndrome were reported in patients treated with REYVOW. Discontinue REYVOW if symptoms of serotonin syndrome occur**
  - **Dosage:**
    - **Recommended dose is 50 mg, 100 mg, or 200 mg taken orally, as needed**
    - **No more than one dose should be taken in 24 hours**
  - **Availability:**
    - **Tablets: 50 and 100 mg**

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Antihypertensives (Angiotensin Modulators, Beta Blockers, Calcium Channel Blockers, Diuretics)

Disease State Description – Antihypertensives

- **Hypertension**
  - Approximately 116.4 million (46%) adults in the United States (US) have hypertension
  - The highest age-related prevalence is among African American men and women at 58.6% and 56%, respectively
  - It is estimated that hypertension is controlled in only 54% of patients with the condition
  - Hypertension is an independent risk factor for cardiovascular disease and can lead to heart failure (HF) and stroke if uncontrolled for a prolonged period
  - Angiotensin receptor blockers (ARBs) are indicated for the treatment of hypertension either alone or in combination with other antihypertensive medications

- **Nephropathy**
  - Approximately 25% of patients with diabetes will develop microalbuminuria during the 10 years after diagnosis and 25% to 40% will develop diabetic nephropathy over 20 to 25 years after diabetes onset
  - Diabetic nephropathy is the most common cause of end-stage renal disease (ESRD) in the U.S., accounting for 40% of all the patients with end-stage renal disease (ESRD) who are on dialysis
  - Type 1 and 2 diabetes increase the risk for nephropathy and follow the same progression to renal insufficiency and failure
  - Guidelines by the American Diabetes Association (ADA; 2019), American Association of Clinical Endocrinologists/American College of Endocrinology (AACE/ACE; 2015/2019), the AHA/American Stroke Association (ASA; 2014), and the JNC-8 suggest that all patients with diabetes should receive an ACE inhibitor or ARB for the treatment of hypertension to reduce the risk of stroke and to delay the progression of diabetic nephropathy

Antihypertensives - Guidelines

- JNC-8, 2014
  - Recommends to start antihypertensive therapy in patients at least 60 years of age when systolic blood pressure (SBP) 150 mm Hg or greater or diastolic blood pressure (DBP) is 90 mm Hg or greater, with a goal of SBP < 150 mm Hg and DBP < 90 mm Hg
  - For patients younger than 60 years and adults with chronic kidney disease (CKD), therapy should be initiated when SBP ≥ 140 mm Hg and DBP ≥ 90 mm Hg and target blood pressure is less than 140/90 mm Hg
  - In the non-African American population, initial treatment should include a thiazide-type diuretic, calcium channel blocker (CCB), angiotensin-converting enzyme (ACE) inhibitor or ARB
  - For African Americans, initial treatment should include a thiazide-type diuretic or CCB
  - In patients with CKD treatment should include an ACE inhibitor or ARB to improve kidney function, regardless of race or diabetes status
  - If blood pressure goal is not reached within 1 month of starting treatment, the dose should be increased or a second a drug from another class should be added; a third drug can be added if needed

Antihypertensives - Guidelines

- The American College of Cardiology (ACC) and American Heart Association (AHA) Joint Guidelines, 2017
  - The guideline revised the classification system for blood pressure
  - The initiation of drug therapy should be based on a combination of average BP, atherosclerotic cardiovascular disease (CVD) risk, and comorbid conditions
    - For high-risk (pre-existing CVD or estimated 10-year risk of ≥ 10%) adults with stage 1 hypertension, defined as average SBP of 130 to 139 mm Hg or DBP 80 to 89 mm Hg, treatment should be initiated in patients with a BP of ≥ 130/80 mm Hg
    - For lower-risk adults, ACC/AHA specifies the threshold BP for drug treatment at ≥ 140/90 mm Hg
    - Regardless of risk, the goal BP after initiating treatment is < 130/80 mm Hg
    - First-line therapy recommendations include thiazide diuretics, CCBs, and ACE inhibitors or ARBs
  - Patients in stage 2 hypertension (SBP ≥ 140 mm Hg or DBP ≥ 90 mm Hg) should be initiated with 2 first-line treatment agents with differing mechanisms of action
  - For hypertension in adults, the ACC/AHA notes that simultaneous use of an ACE inhibitor, ARB, and/or renin inhibitor is potentially harmful and is not recommended
  - For resistant hypertension, AHA provides additional guidance with an initial focuses on optimizing first-line therapies, including ARBs

Antihypertensives - Guidelines

- The AHA, 2018
  - The AHA defines Resistant Hypertension (RH) as above-goal elevated blood pressure (BP) despite concurrent use of 3 antihypertensive drug classes at maximally tolerated doses or BP that requires ≥ 4 medications to achieve a target level
  - Hypertension is typically treated with a diuretic, a long-acting calcium channel blocker, and a renin-angiotensin system blocker (angiotensin-converting enzyme inhibitor [ACEI] or angiotensin receptor blocker [ARB])
  - Similar to the 2017 ACC/AHA BP target of ≤ 130/80 mm Hg in patients on antihypertensive therapy
  - Diagnosis of RH should be made based on a 24-hour ambulatory BP measured after medication adherence has been confirmed
  - RH assessment should consider lifestyle, drug-drug interactions, secondary hypertension, and presence of end organ damage
  - Recommended treatment for confirmed RH includes optimization of lifestyle interventions, use of a long-acting thiazide-like diuretic (e.g., chlorthalidone, indapamide), and addition of a mineralocorticoid receptor antagonist (e.g., spironolactone, eplerenone)
  - If BP remains above target levels, addition of agents with different mechanisms, and possibly referral to a hypertension specialist, are advised

Antihypertensives - Guidelines

- The American College of Cardiology (ACC) and American Heart Association (AHA) Joint Guidelines, 2017
  - The guideline revised the classification system for blood pressure
  - The initiation of drug therapy should be based on a combination of average BP, atherosclerotic cardiovascular disease (CVD) risk, and comorbid conditions
    - For high-risk (pre-existing CVD or estimated 10-year risk of ≥ 10%) adults with stage 1 hypertension, defined as average SBP of 130 to 139 mm Hg or DBP 80 to 89 mm Hg, treatment should be initiated in patients with a BP of ≥ 130/80 mm Hg
    - For lower-risk adults, ACC/AHA specifies the threshold BP for drug treatment at ≥ 140/90 mm Hg
    - Regardless of risk, the goal BP after initiating treatment is < 130/80 mm Hg
    - First-line therapy recommendations include thiazide diuretics, CCBs, and ACE inhibitors or ARBs
  - Patients in stage 2 hypertension (SBP ≥ 140 mm Hg or DBP ≥ 90 mm Hg) should be initiated with 2 first-line treatment agents with differing mechanisms of action
  - For hypertension in adults, the ACC/AHA notes that simultaneous use of an ACE inhibitor, ARB, and/or renin inhibitor is potentially harmful and is not recommended
  - For resistant hypertension, AHA provides additional guidance with an initial focuses on optimizing first-line therapies, including ARBs

Antihypertensives - Guidelines

- <u>The American College of Physicians (ACP) and American Academy of Family Physicians (AAFP), 2017</u>
  - Recommend initiating antihypertensive therapy in adults 60 years and older with SBP ≥ 150 mm Hg with a target SBP < 150 mm Hg to reduce the risk of mortality, stroke, and cardiac events
  - A stricter goal of SBP < 140 mm Hg may be considered
    - In older adults with a history of stroke or transient ischemic attack to reduce the risk for recurrent stroke
    - In older adults at high cardiovascular (CV) risk to reduce the risk of stroke or cardiac events
  - The clinician and patient should discuss the risk versus benefit when determining the most appropriate blood pressure goal
  - The ACP and AAFP also state that providers should consider treatment with nonpharmacologic options (e.g., weight loss, diet, exercise), as well as pharmacologic therapy
  - Treatment burden (e.g., total number of drugs prescribed, drug interactions, adverse effects), given the potential for other comorbid conditions, should also be taken into consideration when treating hypertensive older adults
  - If pharmacologic therapy is chosen, generic formulations should be prescribed, when available, to reduce cost and thereby aid treatment adherence

Antihypertensives - Guidelines

- **Pediatric Hypertension**
  - It is estimated that 3.5% of children and adolescents have hypertension

- <u>American Academy of Pediatrics (APP), 2017</u>
  - Published guidelines on diagnosis, evaluation, and treatment of high blood pressure in children and adolescents
  - The goal of treatment is to achieve a blood pressure that decreases the risk for organ damage in youth and decrease the risk of hypertension in adulthood
  - For children and adolescents on treatment for HTN, the blood pressure goal is < 90th percentile and < 130/80 mmHg
  - Lifestyle modifications such as diet and physical exercise are recommended for the potential benefit to reduce blood pressure
  - First line therapy options
    - Include an ACE inhibitor, ARB, long-acting calcium channel blocker, or thiazide diuretic
    - Treatment should begin a low dosage and titrate as needed
    - A second agent may be added if needed
  - Beta blockers are not recommended as initial pharmacologic treatment in children due to the side effect profile and to follow the therapy recommendations of beta blockers in adults
  - Long-term studies on the safety of antihypertensive medications in children and their impact on future cardiovascular disease are limited

Antihypertensives - Guidelines

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

- Agency for Healthcare Research and Quality (AHRQ), 2011
  - Has published a comparative effectiveness report for the ACE inhibitors, ARBs, and aliskiren]
  - The ACE inhibitors and ARBs appear to have similar long-term effects on blood pressure among individuals with essential hypertension
  - It is possible that aliskiren may be more effective than ACE inhibitors (ramipril), but no differences were found in studies when compared to an ARB (losartan)
  - For mortality and major cardiovascular events, there is insufficient evidence to determine if there are any different effects of ACE inhibitors versus ARBs on these serious outcomes
  - ACEIs have been shown to have a greater risk of cough than ARBs and the direct renin inhibitor

Antihypertensives - Guidelines

- American College of Cardiology (ACC) and American Heart Association (AHA), 2017
  - Guidelines for the management of HF
  - Routine combined use of an ACE inhibitor or angiotensin receptor blockers with a beta-blocker is recommended in all patients with reduced ejection fraction heart failure (HF*r*EF), unless contraindicated
  - Drugs with an indication for HF include many ACE inhibitors and some beta-blockers. ARBs that are indicated for HF when a patient is intolerant to an ACE inhibitor include candesartan (Atacand) and valsartan (Diovan)
  - In addition, for patients with HF*r*EF, diuretics are recommended if fluid retention is present; aldosterone antagonists (spironolactone [Aldactone] and eplerenone [Inspra]) are recommended in patients who also have adequate renal function; and digoxin can be beneficial to decrease hospitalizations due to HF
  - The combination of hydralazine and isosorbide dinitrate is recommended in African Americans with HF*r*EF who are persistently symptomatic with the use of an ACE inhibitor and a beta-blocker
  - The ACC/AHA also recommends the use of ARBs in patients unable to tolerate an ACE inhibitor and in patients with HF following a non-ST-elevated myocardial infarction (NSTEMI) or ST-elevated myocardial infarction (STEMI)

Angiotensin Modulators & Combinations – Indications

Drugs	Generic	Indications
Angiotensin II Receptor Blockers: Single Agents		
azilsartan (Edarbi)	---	▪ Hypertension
candesartan (Atacand)	X	▪ Hypertension (including ages 1 to < 17 years) ▪ Heart failure – (LVEF <40%, NYHA II-IV) to reduce risk of CV death and reduce hospitalizations for HF (in addition to ACE inhibitors or when ACE inhibitors are not tolerated)
eprosartan	---	▪ Hypertension
irbesartan (Avapro)	X	▪ Hypertension ▪ Nephropathy in type 2 diabetic patients
losartan (Cozaar)	X	▪ Hypertension (including ages 6 to 16 years) ▪ Nephropathy in type 2 diabetic patients ▪ Reduce the risk of stroke in hypertensive patients with LVH (not in African American patients)
olmesartan (Benicar)	X	▪ Hypertension
telmisartan (Micardis)	X	▪ Hypertension ▪ 80 mg tablets only: risk reduction of myocardial infarction (MI), stroke, or death from CV causes in patients ≥ 55 years at high risk of developing major CV events who are unable to take ACE inhibitors
valsartan (Diovan)	X	▪ Hypertension (including ages 6 to 16 years) ▪ Treatment of HF (NYHA II-IV) to reduce hospitalizations for HF ▪ Reduction of CV mortality in clinically-stable patients with left ventricular failure or left ventricular dysfunction following MI

Angiotensin Modulators & Combinations – Indications

Drugs	Generic	Indications
Angiotensin II Receptor Blockers: Combination Products		
azilsartan/chlorthalidone (Edarbyclor)	---	▪ Hypertension (first-line therapy in patients requiring multiple agents)
candesartan/HCTZ (Atacand HCT)	X	▪ Hypertension
irbesartan/HCTZ (Avalide)	---	▪ Hypertension (first-line therapy in patients requiring multiple agents)
losartan/HCTZ (Hyzaar)	X	▪ Hypertension (first-line therapy in setting of prompt BP reduction) ▪ Reduce the risk of stroke in hypertensive patients with LVH (not in African American patients)
olmesartan/HCTZ (Benicar HCT)	X	▪ Hypertension
sacubitril/valsartan (Entresto)	X	▪ Reduce the risk of CV death and hospitalization for HF in patients with chronic heart failure (NYHA II-IV) and reduced ejection fraction ▪ Treatment of symptomatic HF with systemic left ventricular systolic dysfunction in pediatric patients ages ≥ 1 year
telmisartan/HCTZ (Micardis HCT)	X	▪ Hypertension
valsartan/HCTZ (Diovan HCT)	X	▪ Hypertension (first-line therapy in patients requiring multiple agents)

Angiotensin Modulators & Combinations – Indications

Drugs	Generic	HTN	CHF	Post-MI	Other Indications
ACE Inhibitors					
benazepril (Lotensin)	**X**	X (Pediatrics age 6-16 yrs)	--	--	--
captopril (Capoten)	**X**	X	X	X (in patients with LVD)	Diabetic Nephropathy in type 1 diabetics
enalapril (Vasotec, Epaned)	**X**	X (Pediatrics age 1 month -16 yrs)	X (or asymptomatic LVD) only tablets	--	--
fosinopril (Monopril)	**X**	X (Pediatrics age 6-16 yrs)	X	--	--
lisinopril (Prinivil, Qbrelis, Zestril)	**X**	X (Pediatrics age 6-16 yrs)	X	X (in hemo-dynamically stable patients)	--
moexipril (Univasc)	**X**	X	--	--	--
perindopril (Aceon)	**X**	X	--	--	In stable CAD, reduces risk of cardiovascular mortality and non-fatal MI
quinapril (Accupril)	**X**	X	X	--	--
ramipril (Altace)	**X**	X	X (post-MI)	--	Reduction of risk of MI, stroke, and death from cardiovascular causes
trandolapril (Mavik)	**X**	X	X (post-MI)	X (in patients with CHF or LVD)	--
Renin Inhibitor					
aliskiren (Tekturna)	**---**	X	--	--	--

Beta Blockers – Indications

Drugs	Generic	Indications
Beta-Blockers: Single Agents		
amlodipine/benazepril (Lotrel)	**X**	• Hypertension (not as initial therapy)
amlodipine/olmesartan (Azor)	**X**	• Treatment of hypertension either alone or in combination with other agents Initial therapy in patients likely to need multiple antihypertensive agents to achieve their blood pressure goals
amlodipine/olmesartan/HCTZ (Tribenzor)	**X**	• Hypertension (not as initial therapy)
amlodipine/perindopril (Prestalia)	**---**	• Treatment of hypertension for patients not adequately controlled on monotherapy • Initial treatment of hypertension in patients who will likely require multiple medications for blood pressure control
amlodipine/telmisartan (Twynsta)	**X**	• Treatment of hypertension alone or in combination with other agents Initial treatment of hypertension in patients who will likely require multiple medications for blood pressure control
amlodipine/valsartan (Exforge)	**X**	• Initial treatment of hypertension in patients who will likely require multiple medications for blood pressure control Treatment of hypertension for patients not adequately controlled on monotherapy
amlodipine/valsartan/HCTZ (Exforge HCT)	**X**	• Hypertension (not initial therapy)
nebivolol/valsartan (Byvalson)	**---**	• Hypertension, as initial therapy and in patients not adequately controlled on the individual components
verapamil sustained-release (SR) /trandolapril (Tarka)	**X**	• Hypertension (not as initial therapy)

Beta Blockers – Indications

Drugs	Generic	Indications
Beta-Blockers: Single Agents (*Continued*)		
acebutolol (Sectral)	X	• Hypertension (HTN) • Ventricular arrhythmias
atenolol (Tenormin)	X	• Angina pectoris • HTN • Myocardial infarction (MI)
betaxolol	X	• HTN
bisoprolol	X	• HTN
carvedilol (Coreg)	X	• Mild to severe heart failure (HF), to reduce the risk of hospitalization and improve survival • HTN • Reduce risk of death following MI with left ventricular dysfunction (LVD) in patients with or without HF symptoms
carvedilol (Coreg CR)	X	
labetalol	X	• HTN
metoprolol succinate ER (Toprol XL, Kapspargo Sprinkle)	X	• Angina pectoris • HF – New York Heart Association (NYHA) Class II or III • HTN
metoprolol tartrate (Lopressor)	X	• Angina pectoris • HTN • MI
nadolol (Corgard)	X	• Angina pectoris • HTN
nebivolol (Bystolic)	---	• HTN
pindolol	X	• HTN

Beta Blockers – Indications

Drugs	Generic	Indications
Beta-Blockers: Single Agents (*Continued*)		
propranolol	X	• Angina pectoris • Cardiac arrhythmias • Essential tremor • HTN • Hypertrophic subaortic stenosis • Migraine prophylaxis • MI • Pheochromocytoma
propranolol (Hemangeol)	---	• Proliferating infantile hemangioma requiring systemic therapy
propranolol ER (Innopran XL)	---	• HTN
propranolol ER (Inderal XL)	---	• HTN
propranolol LA (Inderal LA)	X	• Angina pectoris • HTN • Hypertrophic subaortic stenosis • Migraine prophylaxis
sotalol (Betapace)	X	• Ventricular arrhythmias
sotalol (Betapace AF)	X	• Maintenance of normal sinus rhythm in atrial fibrillation/flutter
sotalol (Sotylize)	---	• Ventricular arrhythmias • Maintenance of normal sinus rhythm in atrial fibrillation/flutter
timolol	X	• HTN • Migraine prophylaxis • MI

Drugs	Generic	Indications
Beta-Blockers: Combination Products with Diuretics		
atenolol / chlorthalidone (Tenoretic)	X	• HTN
bisoprolol / hydrochlorothiazide (Ziac)	X	• HTN
metoprolol succinate / hydrochlorothiazide (Dutoprol)	X	• HTN
metoprolol tartrate / hydrochlorothiazide	X	• HTN
nadolol / bendroflumethiazide (Corzide)	X	• HTN
propranolol / hydrochlorothiazide	X	• HTN

Calcium Channel Blockers – Indications

Drugs	Generic	Vasospastic Angina	Angina	Ventricular Rate Control	Hypertension
Dihydropyridines					
amlodipine (Norvasc)	X	X	X	--	X
amlodipine (Katerzia)	---	X	X	--	X
felodipine ER (Plendil)	X	--	--	--	X
Isradipine	X	--	--	--	X
nicardipine (Cardene)	X	--	X	--	X
nicardipine SR (Cardene SR)	X	--	--	--	X
nifedipine (Procardia)	X	X	X	--	--
nifedipine ER, nifedipine SA, nifedipine SR (Adalat CC, Afeditab CR, Nifediac CC, Nifedical XL, Procardia XL)	X	X	X	--	X
Nimodipine	X	--	--	--	--
nimodipine (Nymalize)	---	--	--	--	--
nisoldipine ER (Sular)	X	--	--	--	X

Calcium Channel Blockers – Indications

Drugs	Generic	Vasospastic Angina	Angina	Ventricular Rate Control	Hypertension
Non-dihydropyridines					
diltiazem (Cardizem)	X	X	X	X	--
diltiazem ER (Cardizem LA, Matzim LA)	X	--	X	--	X
diltiazem ER (Cardizem CD, Cartia XT, Dilacor XR, Dilt CD, Taztia XT, Tiazac)	X	X	X	--	X
diltiazem ER (Dilt XR)	X	--	X	--	X
diltiazem ER (Diltia XT)	X	--	X	--	X
verapamil (Calan)	X	X	X	X	X
verapamil ER (Covera-HS)	---	--	X	--	X
verapamil ER (Verelan PM)	X	--	--	--	X
verapamil SR (Calan SR, Isoptin SR, Verelan)	X	--	--	--	X

- **Angina**
  - CCBs improve clinical symptoms and are well tolerated
  - Long-acting CCBs are recommended for the treatment of unstable angina when beta-blockers are not tolerated or do not relieve symptoms
  - Vasospastic (or Prinzmetal's) angina is effectively treated with CCBs by reducing the frequency of anginal attacks

Overview of Disease State – Diuretics

- See Diuretics Appendix

Magellan Rx MANAGEMENT℠

Magellan Medicaid Administration

Cardiovascular Agents (Coronary Vasodilators, Sinus Node Inhibitors, and Pulmonary Hypertension Agents)

Coronary Vasodilators

Magellan Medicaid Administration

Disease State Description – Coronary Vasodilators

- Angina pectoris (AP)
  - A clinical syndrome of coronary artery disease
  - It is caused by decreased oxygen delivery to myocardial tissue. It presents as chest discomfort, including burning, heaviness, or a sensation of choking, or pain in the jaw, neck, ear, and shoulder
  - Symptoms may also include nausea, shortness of breath, or sweating
  - It is associated with an increased risk of cardiac death and myocardial infarction

- Nitrates (nitroglycerin and isosorbide)
  - Approved to treat or prevent AP, caused by coronary artery disease, include immediate-release and extended-release oral tablets, translingual spray, sublingual tablets, and transdermal ointment and patches
  - Lingual formulations of nitroglycerin are used to relieve the symptoms of an acute attack as first-line therapy; they can also be taken prior to engaging in activities that may precipitate an acute attack
  - Relax vascular smooth muscle causing venous and arterial dilation
    - This vasodilation leads to pooling of venous blood and decreased venous return to the heart (preload), reduction in systemic and pulmonary arterial pressure (afterload), and reduced cardiac output
    - By decreasing preload and afterload, myocardial tissue oxygen demand is reduced and pain of angina pectoris is improved
  - Poorly absorbed in the gastrointestinal tract; however, it has good absorption via transmucosal and transdermal routes
    - In general, nitroglycerin has a faster onset and shorter duration of action compared to isosorbide formulations
    - Isosorbide mononitrate is the major active metabolite of isosorbide dinitrate
    - Unlike the dinitrate, it is nearly completely bioavailable and has no active metabolites

Vasodilators, Coronary- Indication, Dosage, and Availability

Drug	Generic	Indication	Dosage	Availability
isosorbide dinitrate (Isordil)	X	Prevention of angina pectoris due to coronary artery disease	Initial: Take 5 to 20 mg 2 to 3 times daily Maintenance: 10 to 60 mg 2 to 3 times daily; Do not exceed 480 mg/day	Tablets: 5, 10, 20, 30 mg Isordil Titradose tablets: 5, 40 mg
Isosorbide dinitrate ER (Isochron, IsoDitrate ER, Dilatrate-SR)	---		Take 40 mg by mouth twice daily; at least 18 hours apart; Do not exceed 160 mg/day	ER tablets and capsules: 40 mg
isosorbide mononitrate	X		20 mg twice daily, with doses given 7 hours apart; 5 mg may be given to patients with small stature; Do not exceed 40 mg/day	Tablets: 10, 20 mg
isosorbide mononitrate ER	X		30 to 60 mg once daily, preferably in the morning upon awakening; increased to 120 mg; Do not exceed 240 mg/day	ER tablets: 30, 60, 120 mg
nitroglycerin ER (Nitro-Time)	X		Take 2.5 to 6.5 mg 3 to 4 times daily; titrate to clinical response and adverse reactions as needed	ER capsules: 2.5, 6.5, 9 mg
nitroglycerin lingual (NitroMist, Nitrostat, Nitrolingual Pumpspray)	X	Acute relief of an attack or acute prophylaxis of angina pectoris due to coronary artery disease	**Acute relief:** • Translingual spray: 1 to 2 sprays on or under the tongue, may repeat as needed every 5 minutes up to 3 sprays in 15 minutes • Sublingual tablets: 1 tablet dissolved under the tongue or in the buccal pouch immediately following indication of anginal attack, may repeat every 5 minutes up to 3 doses in 15 minutes **Prophylaxis of angina pectoris:** Use 5 to 10 minutes prior to engaging in activities that might precipitate an acute attack	Translingual aerosol spray: 400 mcg/spray in packages containing 90 or 230 doses Lingual metered pumpspray: 400 mcg/spray in packages containing 60 or 200 doses Sublingual tablets: 0.3, 0.4, 0.6 mg
nitroglycerin lingual (NitroMist)	---			Translingual aerosol spray: ▪ 400 mcg/spray in packages containing 90 or 230 doses

Vasodilators, Coronary- Indication, Dosage, and Availability

Drug	Generic	Indication	Dosage	Availability
nitroglycerin ointment (Nitro-Bid)	---	Prevention of angina pectoris due to coronary artery disease	Apply 7.5 mg (1/2 inch) to 30 mg (2 inches) twice a day, onto 36 square inches of hairless area of skin (chest, abdomen, thighs); applied on rising in the morning and 6 hours later; The dose may be doubled, and even doubled again, if tolerance occurs	Nitro-Bid 2% topical ointment: 30 gram, 60 gram ; 48 x 1 gram unit dose packets
nitroglycerin sublingual powder (GoNitro)	---	Acute relief of an attack or acute prophylaxis of angina pectoris due to coronary artery disease	Acute relief: ▪ Sublingual powder: 1 to 2 packets under the tongue, may repeat once after 5 minutes, up to 3 packets in 15 minutes ▪ Sublingual tablets: 1 tablet dissolved under the tongue or in the buccal pouch immediately following indication of anginal attack, may repeat every 5 minutes up to 3 doses in 15 minutes Prophylaxis of angina pectoris: ▪ Use 5 to 10 minutes prior to engaging in activities that might precipitate an acute attack	Sublingual powder: ▪ 400 mcg packet
nitroglycerin sublingual tablets (Nitrostat)	X			Sublingual tablets: ▪ 0.3 mg, 0.4 mg, 0.6 mg
nitroglycerin transdermal (Minitran, Nitro-Dur)	X	Prevention of angina pectoris due to coronary artery disease	Apply 1 patch topically every 24 hours; leave the patch on for 12 to 14 hours, then remove for 10 to 12 hours prior to applying the next patch	Patch: 0.1, 0.2, 0.3, 0.4, 0.6, 0.8 mg/hr

Vasodilators, Coronary- Guidelines

- American College of Physicians/American College of Cardiology Foundation/American Heart Association/American Association for Thoracic Surgery/Preventive Cardiovascular Nurses Association/Society of Thoracic Surgeons, 2012
  - Relief of symptoms in patients with stable IHD
    - β-blockers should be prescribed as initial therapy
    - Calcium-channel blockers or long-acting nitrates should be prescribed when β-blockers are contraindicated or cause unacceptable side effects
    - Calcium-channel blockers or long-acting nitrates, in combination with β-blockers, should be prescribed when initial treatment with β-blockers is unsuccessful
    - The organizations recommend that sublingual nitroglycerin or nitroglycerin spray should be used for immediate relief of angina
  - Sublingual nitroglycerin tablets or translingual spray are drugs of choice to abort acute anginal attacks and prophylactically to prevent angina due to activity

Sinus Node Inhibitors

Magellan Medicaid Administration

Disease State Description – Sinus Node Inhibitors

- Heart failure is a progressive syndrome caused by a change in cardiac structure or cardiac function resulting in a failure of the heart to deliver an adequate supply of oxygenated blood to the tissues
  - Coronary artery disease (CAD) is the cause of heart failure in about 75% of cases
  - The incidence of heart failure in the US exceeds 5 million; many of these patients are over the age of 70
- Typical symptoms include dyspnea, fatigue, and fluid retention
- In response to a decrease in cardiac output, a number of compensatory mechanisms occur, such as an activation of the sympathetic nervous system (SNS) and the renin-angiotensin-aldosterone system (RAAS)
- Goals of treatment include improving patient symptoms, slowing disease progression, and prolonging survival
  - Overall, 5-year survival is approximately 50% for all patients with a heart failure diagnosis, with survival declining with increased disease symptoms and severity
  - Mortality rates have declined over the last few decades due to improved pharmacotherapy, including the use of agents to antagonize the SNS and RAAS effects such as beta-blockers, angiotensin converting enzyme (ACE) inhibitors, and angiotensin receptor blockers (ARBs)
- Ivabradine (Corlanor) inhibits the diastolic I_f current in the sinoatrial (SA) node resulting in a dose-dependent reduction in heart rate
  - Unlike beta-blockers, ivabradine has no negative inotropic effects

Sinus Node Inhibitors-Indication, Dosing, and Availability

Drug	Indication	Dosing	Availability
Ivabradine (Corlanor)	Reduce the risk of hospitalization for worsening heart failure in patients with stable, symptomatic chronic heart failure with left ventricular ejection fraction ≤ 35% who are in sinus rhythm with resting heart rate ≥ 70 beats per minute (bpm) and either are on maximally tolerated doses of beta-blockers or have a contraindication to beta-blocker use Treatment of stable, symptomatic heart failure due to dilated cardiomyopathy (DCM) in pediatric patients ≥ 6 months old	5 mg twice daily with meals; titrate to maximum of 7.5 mg twice daily	5 mg, 7.5 mg tablet 5 mg/5 mL oral solution

Sinus Node Inhibitors-Guidelines

- American College of Cardiology (ACC), American Heart Association (AHA), and Heart Failure Society of American (HFSA), 2017
  - Can be beneficial to reduce heart failure hospitalization in patients with symptomatic (NYHA class II-III) stable chronic HFrEF (LVEF ≤ 35%) who are receiving guideline-directed evaluation and management, including beta blocker at maximum tolerated dose, and with a heart rate of ≥ 70 bpm at rest and who are in sinus rhythm

Pulmonary Hypertension

Magellan Medicaid Administration

Disease State Description - Pulmonary Arterial Hypertension

- The prevalence varies substantially depending on the type, etiology, and underlying condition; estimated to be ~15 per million people
- Pulmonary hypertension (PH) is characterized by an increase in pulmonary arterial pressure and secondary right ventricular failure. This is defined as a resting mean pulmonary arterial pressure (mPAP) ≥ 25 mm Hg
- Symptoms include dyspnea, dizziness, syncope, fatigue, edema (peripheral), angina, palpitations, and other symptoms, all of which are exacerbated by exertion
- PH does not have a cure and, if left untreated, PH is a life-threatening disease with poor prognosis
- Management of PH should be limited to specialized centers where clinicians are experienced in the evaluation and treatment of patients with PH
- Although the number of approved therapies for PAH has grown in the past years, the prognosis is still poor, with approximately 50% mortality within the first 5 years after diagnosis

Disease State Description - Pulmonary Arterial Hypertension

- There are many causes of PAH including idiopathic or underlying disease and hereditary causes
  - Cellular changes in the walls of pulmonary arteries, and it appears that mutations in the bone morphogenetic protein receptor type 2 (BMPR2) gene plays a key role in the pathogenesis of heritable PAH
  - Other etiologies in PAH include drugs and toxins, collagen vascular resistance, human immunodeficiency virus (HIV), portal hypertension, chronic thromboembolism, and congenital heart disease
- The World Health Organization (WHO) classifies PH patients into 5 groups based on etiology
  - Group I now refers to pulmonary arterial hypertension (PAH)
  - Group II refers to PH due to left heart disease
  - Group III refers to PH due to lung disease
  - Group IV refers to PH due to blood clots in the lungs
  - Group V refers to refers to PH due to blood and other rare disorders
- In 2013, clinical classifications were updated to provide the same PH classifications for adult and pediatric patients. In addition, the individual categorization of the persistent PH of neonates (PPHN) was included

Pulmonary Arterial Hypertension – Indications

Drug	Generic	Indication(s)
Oral Agents		
ambrisentan (Letairis)	**X**	• Treatment of pulmonary arterial hypertension (World Health Organization [WHO] Group I) to improve exercise ability and delay clinical worsening • In combination with tadalafil to reduce the risks of disease progression and hospitalization for worsening PAH, and to improve exercise ability
bosentan (Tracleer)	**X**	• Treatment of pulmonary arterial hypertension (WHO Group I) in patients with WHO Class II to IV symptoms, to improve exercise ability and decrease clinical worsening • Treatment of idiopathic or congenital PAH to improve pulmonary vascular resistance (PVR) in pediatric patients age 3 years and older which is expected to result in an improvement in exercise ability
macitentan (Opsumit)	**---**	• Treatment of pulmonary arterial hypertension (WHO Group I) to delay disease progression which includes death, initiation of intravenous (IV) or subcutaneous (SC) prostanoids, or clinical worsening; Opsumit also reduced hospitalization for PAH
riociguat (Adempas)	**---**	• Persistent/recurrent chronic thromboembolic pulmonary hypertension (CTEPH) (WHO Group IV) after surgical treatment or inoperable CTEPH to improve exercise capacity and WHO functional class • Pulmonary arterial hypertension (WHO Group I) to improve exercise capacity, improve WHO functional class and to delay clinical worsening
selexipag (Uptravi)	**---**	• Treatment of pulmonary arterial hypertension (WHO Group I) to delay disease progression and reduce the risk of hospitalization for PAH
sildenafil (Revatio)	**X**	• Treatment of pulmonary arterial hypertension (WHO Group I) to improve exercise ability and delay clinical worsening
tadalafil (Adcirca)	**X**	• Treatment of pulmonary arterial hypertension (WHO Group I) to improve exercise ability
treprostinil (Orenitram)	**---**	• Treatment of pulmonary arterial hypertension (WHO Group I) to improve exercise capacity
Inhalation Agents		
iloprost (Ventavis)	**---**	• Treatment of pulmonary arterial hypertension (WHO Group I) to improve a composite endpoint consisting of exercise tolerance, symptoms (NYHA Class), and lack of deterioration
treprostinil (Tyvaso)	**---**	• Treatment of pulmonary arterial hypertension (WHO Group I) to increase exercise ability

Pulmonary Arterial Hypertension – Indications

Drug	Generic	Indication(s)
Prostanoids		
epoprostenol (Flolan)	**X**	Treatment of pulmonary arterial hypertension (WHO Group I) to improve exercise capacity; Studies establishing effectiveness included predominantly patients with NYHA Functional Class III-IV symptoms and etiologies of idiopathic or heritable PAH or PAH associated with connective tissue diseases
epoprostenol (Veletri)	**---**	Treatment of pulmonary arterial hypertension (WHO Group 1) to improve exercise capacity; Studies establishing effectiveness included predominantly patients with NYHA Functional Class III-IV symptoms and etiologies of idiopathic or heritable PAH or PAH associated with connective tissue diseases
treprostinil (Remodulin)	**X**	Treatment of pulmonary arterial hypertension (WHO Group 1) to diminish symptoms associated with exercise; Studies establishing effectiveness included patients with NYHA Functional Class II-IV symptoms and etiologies of idiopathic or heritable PAH (58%), PAH associated with congenital systemic-to-pulmonary shunts (23%), or PAH associated with connective tissue diseases (19%) Patients who require transition from Flolan, to reduce the rate of clinical deterioration. The risks and benefits of each drug should be carefully considered prior to transition
Phosphodiesterase type 5 (PDE-5) inhibitor		
sildenafil (Revatio)	**X**	Treatment of pulmonary arterial hypertension (WHO Group I) in adults to improve exercise ability and delay clinical worsening; Studies establishing effectiveness were short-term (12 to 16 weeks), and included predominately patients with NYHA Functional Class II-III symptoms and idiopathic etiology (71%) or associated with connective tissue disease (25%) Limitation of Use: Adding sildenafil to bosentan therapy does not result in any beneficial effect on exercise capacity

Pulmonary Arterial Hypertension – Guidelines

- Treatment Guidelines, European Society of Cardiology (ESC) and the European Respiratory Society (ERS), February 2016
  - **At the time of diagnosis of PAH**, the **suggested initial approach is the adoption of general measures** (exercise training, psychosocial support, rehabilitation) **and the initiation of supportive therapy** (oral anticoagulation, diuretics, digoxin, and long-term oxygen therapy, if needed
  - **Patients who are at low or intermediate risk for 1-year mortality can be treated with either initial monotherapy or initial oral combination therapy**
  - **If initial monotherapy** is chosen, **no evidence-based first-line monotherapy can be proposed** because there are no head-to-head comparisons
  - If **initial combination therapy** is chosen, **ambrisentan plus tadalafil has been given a higher grade recommendation** because the combination has proven to be superior to initial ambrisentan or tadalafil monotherapy in delaying clinical failure

Treatment Guidelines, European Society of Cardiology (ESC) and the European Respiratory Society (ERS), February 2016

Therapy	Recommendation	Strength of Recommendation
Initial monotherapy	WHO-FC II: ambrisentan (Letairis), bosentan (Tracleer), macitentan (Opsumit), sildenafil (Revatio), tadalafil (Adcirca), riociguat (Adempas), and selexipag (Uptravi) WHO-FC III: ambrisentan, bosentan, macitentan, sildenafil, tadalafil, riociguat, selexipag, IV epoprostenol (Flolan®/Veletri®), inhaled iloprost (Ventavis), SC or inhaled treprostinil (Remodulin®, Tyvaso) and oral or IV treprostinil (Orenitram, Remodulin) WHO-FC IV: IV epoprostenol (Level I, Grade A), ambrisentan, bosentan, macitentan, sildenafil, tadalafil, riociguat, inhaled iloprost, SC, IV or inhaled treprostinil	Level I, Grade A or B for all Level I, Grade A or B Level IIa or IIb, Grade B or C for treprostinil Level IIb, Grade C
Initial combination therapy	WHO-FC II: • Ambrisentan + tadalafil • Other endothelin receptor antagonist (ERA) + phosphodiesterase type 5 inhibitor (PDE-5i) WHO-FC III: • Ambrisentan + tadalafil • Other ERA + PDE-5i, bosentan + sildenafil + IV epoprostenol, bosentan + IV epoprostenol, other ERA or PDE-5i + SC treprostinil, other ERA or PDE-5i + other IV prostacyclin analogues WHO-FC IV: • Ambrisentan + tadalafil • Other ERA + PDE-5i, bosentan + sildenafil + IV epoprostenol, bosentan + IV epoprostenol, other ERA or PDE-5i + SC treprostinil, other ERA or PDE-5i + other IV prostacyclin analogues	Grade I, Level B Grades IIa, Grade C Grade I, Level B Grades IIa, or IIb Grade C Grades IIa, or IIb Grade C

Pulmonary Arterial Hypertension – Guidelines

- American College of Chest Physicians (CHEST), 2014 (Updated 2018)
  - At the time of diagnosis of PAH
    - The suggested **initial approach** is
      - **Treatment of contributing causes of PAH** (e.g., sleep apnea, systemic hypertension)
      - The **adoption of general measures** (supervised exercise activity, influenza and pneumonia vaccinations, and avoidance of pregnancy, high altitudes, and non-essential surgery)
      - The **initiation of supportive therapy** (oxygen therapy if needed to maintain oxygen saturations > 91%)
      - Palliative care
  - Unless there is a contraindication, acute vasoreactivity testing should be performed at a facility with experience in performing and interpreting the test (UCBS)
    - **A trial of high dose oral calcium channel blockers (CCB), such as amlodipine, diltiazem, or nifedipine, is recommended in patients with a positive acute vasoreactive test**
    - Furthermore, **CCBs should not be used empirically to treat PAH** in the absence of demonstrated acute vasoreactivity (UCBS)
    - Patients should be followed closely for response and side effects of therapy. Alternative or additional PAH therapy should be initiated if improvement to WHO FC I or II are not seen after the trial of a CCB

Pulmonary Arterial Hypertension – Guidelines

- American College of Chest Physicians (CHEST), 2014 (Updated 2018)
  - In treatment-naive patients who are not candidates for, or who have failed CCB therapy, treatment is based on WHO functional class (UCBS)
    - In treatment-naïve patients with WHO FC I
      - Continued monitoring for disease progression is advised (UCBS)
    - **In treatment-naïve patients with WHO FC II**
      - **Initial combination therapy with ambrisentan and tadalafil to improve 6-minute walk distance (6MWD) is suggested (weak recommendation, moderate quality evidence)**
      - **In patients who are unwilling to take or cannot tolerate combination therapy, then monotherapy with ambrisentan, sildenafil (strong recommendations, low quality evidence for both), bosentan, macitentan, tadalafil, or riociguat (UCBS for all 4 products) is recommended**
    - **In treatment-naïve patients with WHO FC III without rapid disease progression or poor prognosis**
      - **Initial combination therapy with ambrisentan and tadalafil to improve 6MWD is suggested (weak recommendation, moderate quality evidence)**
      - **In patients who are unwilling to take or cannot tolerate combination therapy, then monotherapy with ambrisentan, bosentan, sildenafil (strong recommendations, low or moderate quality to improve 6MWD for all 3 products), macitentan, tadalafil, or riociguat (UCBS for all 3 products) is recommended**
    - For treatment-naïve patients with WHO FC IV
      - Initial therapy with a parenteral prostanoid agent is recommended (UCBS)
      - In patients who cannot comply with parenteral administration, inhaled prostanoid in combination with an oral endothelin receptor antagonist or an oral PDE-5 inhibitor are alternatives (UCBS)

Magellan Rx MANAGEMENT℠

Magellan Medicaid Administration

Bone Density Regulators (Bone Resorption Suppression and Related Agents)

Disease State Description - Bone Resorption Inhibitors

- Osteoporosis is characterized by the deterioration of bone tissue and low bone mass
- Approximately 10 million Americans have the diagnosis of osteoporosis, and an additional 43 million have low bone mass, placing them at increased risk for this disease
  - As many as 1 in 2 women and 1 in 5 men are at risk for an osteoporosis-related fracture during their lifetime
  - Approximately 1 in 4 men in the U.S. over the age of 50 will have an osteoporosis-related fracture in his remaining lifetime
  - Osteoporosis is common in all racial groups but is most common in Caucasians
- There are 3 categories of osteoporosis:
  - Postmenopausal
    - Postmenopausal osteoporosis affects mainly trabecular bone in the decade after menopause as estrogen deficiency increases bone resorption more than bone formation
  - Age-related
    - Age-related osteoporosis results from increased bone resorption that begins shortly after peak bone mass is obtained. Cortical and trabecular bone are both affected.
  - Secondary osteoporosis
    - Caused by medications (glucocorticoids, excess thyroid replacement, some antiepileptic drugs, and long-term heparin use) or diseases (hyperthyroidism, type 1 diabetes)

National Osteoporosis Foundation, 2015

Bone Resorption Inhibitors – Indications

Drugs	Generic	Indication(s)
Bisphosphonates		
alendronate (Binosto)	---	• Treatment and prevention of osteoporosis in postmenopausal women • Treatment to increase bone mass in men with osteoporosis
alendronate (Fosamax)	X	• Treatment and prevention of osteoporosis in postmenopausal women • Treatment to increase bone mass in men with osteoporosis • Treatment of glucocorticoid-induced osteoporosis in men and women receiving glucocorticoids in a daily dosage equivalent of 7.5 mg or greater of prednisone and who have low bone mineral density • Treatment of Paget's disease of bone in men and women
alendronate/ vitamin D (Fosamax Plus D)	---	• Treatment of osteoporosis in postmenopausal women • Treatment to increase bone mass in men with osteoporosis
etidronate	X	• Treatment of Paget's disease of bone • Prevention and treatment of heterotopic ossification following total hip replacement or spinal cord injury
ibandronate (Boniva)	X	• Treatment and prevention of osteoporosis in postmenopausal women
risedronate (Actonel)	X	• Treatment and prevention of osteoporosis in postmenopausal women • Treatment to increase bone mass in men with osteoporosis • Prevention and treatment of glucocorticoid-induced osteoporosis in men and women who are either initiating or continuing systemic glucocorticoids in a daily dosage equivalent of 7.5 mg or greater of prednisone for chronic diseases • Treatment of Paget's disease of bone in men and women
risedronate delayed-release (Atelvia)	X	• Treatment of osteoporosis in postmenopausal women
Calcitonins		
calcitonin-salmon	X	• Treatment of postmenopausal osteoporosis in females greater than 5 years postmenopause when alternative treatments are not suitable. Fracture reduction efficacy has not been demonstrated.

Bone Resorption Inhibitors – Indications

Drugs	Generic	Indication(s)
Others		
abaloparatide (Tymlos)	---	• Treatment of osteoporosis in postmenopausal women who are at high risk for fractures •
denosumab (Prolia)	---	• Treatment of osteoporosis in postmenopausal women at high risk for fracture, defined as a history of osteoporotic fracture, or multiple risk factors for fracture, or in patients who have failed or are intolerant to other available osteoporosis therapy • Treatment of osteoporosis associated with newly initiated or sustained systemic glucocorticoid therapy in men and women at high risk for fracture. • Treatment of bone loss in men with prostate cancer on androgen deprivation therapy • Treatment of bone loss in women undergoing breast cancer therapy with adjuvant aromatase therapy • Treatment to increase bone mass in men diagnosed with osteoporosis and a high fracture risk who have failed or are intolerant to other potential therapies
raloxifene (Evista)	**X**	• Treatment and prevention of osteoporosis in postmenopausal women • Reduction in risk of invasive breast cancer in postmenopausal women who either have osteoporosis or are at high risk for invasive breast cancer
teriparatide (Forteo)	---	• Treatment of osteoporosis in postmenopausal women who are at high risk for fractures • Increase of bone mass in men with primary or hypogonadal osteoporosis who are at high risk for fractures • Treatment of men and women with osteoporosis associated with sustained systemic glucocorticoid therapy at high risk for fracture
romosozumab-aqqg (Evenity)	---	• Treatment of osteoporosis in postmenopausal women at high risk for fracture, defined as a history of osteoporotic fracture, or multiple risk factors for fracture; or patients who have failed or are intolerant to other available osteoporosis therapy

Guidelines - Bone Resorption Inhibitors

- North American Menopause Society (NAMS), 2010
  - Recommends bisphosphonates as first-line drugs to treat postmenopausal women with osteoporosis (defined as having a T-score ≤ -2.5)
  - Calcitonin is not a first-line drug for postmenopausal osteoporosis treatment; however, it is an option for women with osteoporosis who are more than 5 years beyond menopause
  - Pharmacologic options approved for the treatment of postmenopausal osteoporosis include denosumab, teriparatide, and calcitonin
  - Pharmacologic options approved for the prevention and treatment of postmenopausal osteoporosis include bisphosphonates and the estrogen agonist/antagonist raloxifene
  - They note that there is controversy regarding the optimal duration of bisphosphonate therapy and the length of a “drug holiday” and state that these should be based on an individualized assessment of risk and benefit
  - Abaloparatide (Tymlos) was not available at the time of these publications

Guidelines - Bone Resorption Inhibitors

- National Osteoporosis Foundation (NOF), 2014
  - Recognize all FDA-approved medications for the prevention and/or treatment of osteoporosis as possible options
  - Treatment agent of choice should be based on available clinical information in addition to intervention thresholds
  - Duration of pharmacologic therapy should be specific to each individual with the need for continuation of medications reviewed on an annual basis

- American Association of Clinical Endocrinologists (AACE) and American College of Endocrinology (ACE), 2016
  - Recommend alendronate, risedronate, zoledronic acid, and denosumab as initial therapy for most patients at high risk of fracture
  - Teriparatide, denosumab, or zoledronic acid should be considered for patients unable to use oral therapy and as initial therapy for patients at especially high fracture risk
  - Raloxifene or ibandronate may be appropriate initial therapy in some cases where patients requiring drugs with spine-specific efficacy
  - The guidelines also stated few patients are using calcitonin as long-term treatment for osteoporosis because more effective agents are available to increase bone density and reduce fracture risk
  - Abaloparatide (Tymlos) was not available at the time of these publications

Guidelines - Bone Resorption Inhibitors

- American College of Physicians (ACP), 2017 (an update on the 2008 guidelines)
  - Recommends physicians offer pharmacologic treatment to reduce the risk for hip and vertebral fractures in women with known osteoporosis and treatment should occur for 5 years
  - However, they recommend against bone density monitoring during the 5-year treatment period
  - ACP recommends against using menopausal estrogen or estrogen with progesterone or raloxifene for osteoporosis treatment in women
  - They further state that treatment decisions in older osteopenic women (≥ 65 years old) who are at a high risk of fracture should be based on a discussion with the patient regarding her preference, fracture risk and treatment benefits, harms, and cost
  - Regarding therapy in men, they recommend that clinicians offer treatment with bisphosphonates to reduce the risk of vertebral fractures in those with clinical osteoporosis
  - These guidelines are based on a systematic review of literature and evidence for specific pharmacotherapy treatments which are detailed in the publication
  - Abaloparatide (Tymlos) was not available at the time of these publications

Guidelines - Bone Resorption Inhibitors

- Endocrine Society, 2019
  - Recommend pharmacologic therapy for postmenopausal women at high risk of fracture, especially those with recent fracture
  - This populations should be treated initially with a bisphosphonate or denosumab to reduce fracture risk
  - However, ibandronate is not recommended to reduce the risk of nonvertebral or hip fracture
  - For postmenopausal women with a very high risk of fracture, the guidelines recommend starting with either teriparatide or abaloparatide for up to 2 years of treatment before switching to a bisphosphonate or denosumab to maintain bone density
  - Raloxifene, calcitonin, and hormone replacement therapy are only recommended if patients are not appropriate candidates for treatment with bisphosphonates or denosumab and do not have any other contraindications to these therapies
  - Romosozumab-aqqg (Evenity) was FDA approved in April 2019. Its use for the treatment of osteoporosis in postmenopausal women has not yet been addressed by any guideline at this time

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Antiemetics/Antivertigo Agents

Disease State Description – Antiemetic Agents

- Chemotherapy-induced vomiting (emesis) and nausea can significantly impact a patient's quality of life, leading to poor compliance with future chemotherapy or radiation treatments
- In addition, nausea and vomiting can lead to several adverse events, such as nutrient depletion, metabolic imbalances, erosion of self-care, anorexia, diminished performance and mental status, wound dehiscence, tears in the esophagus, and cessation of potentially useful or curative cancer treatment
- Approximately 70% to 80% of all cancer patients receiving chemotherapy experience nausea and/or vomiting, whereas 10% to 44% experience anticipatory nausea and/or vomiting
- Furthermore, more than 90% of patients using highly emetogenic chemotherapeutic agents will experience acute emesis; however, only approximately 30% of these patients will experience a vomiting episode if they receive an antiemetic prior to their highly emetogenic chemotherapeutic treatment

National Comprehensive Cancer Network, 2017

Disease State Description - Antiemetic Agents

- Motion sickness
  - Result of a conflict between the various senses in regard to motion
  - The overall incidence of dizziness, vertigo, and imbalance is 5% to 10%
  - There are multiple causes of vertigo, such as head trauma, cerebellar lesions, vestibular disease, or migraine
  - Symptoms include nausea, vomiting, pallor, sweating, and often a sense of impending doom
  - There are both non-pharmacologic and pharmacologic interventions for the prevention or management of motion sickness
    - None are ideal, and the medications typically cause drowsiness or similar adverse effects
    - Symptomatic treatment of motion sickness generally includes the use of antihistamines, benzodiazepines, or antiemetics
    - Vestibular rehabilitation in select patients may be used with a goal of treating the underlying cause

- Nausea and vomiting of pregnancy ("morning sickness")
  - Can occur at any time of day and can affect pregnant women with varying symptoms from nausea to severe vomiting
  - Lifestyle changes for women with nausea and vomiting of pregnancy include rest, avoiding nauseating stimuli, eating small, frequent low fat meals that are low in spices

Centers for Disease Control and Prevention, 2010

The Medical Letter, 2013

Antivertigo Agents – Indications

Drugs	Generic	Indication(s)
Anticholinergics		
scopolamine (Transderm Scop)	X	▪ Treatment and prevention of motion sickness ▪ Prevention of postoperative nausea/vomiting (N/V) ▪ Treatment of N/V
Antihistamines		
dimenhydrinate (Dramamine)	X	▪ Treatment and prevention of motion sickness ▪ Treatment of N/V
diphenhydramine (Benadryl)	X	▪ Treatment and prevention of N/V associated with motion sickness
meclizine (Antivert, Bonine, Dramamine Less Drowsy)	X	▪ Treatment and prevention of N/V associated with motion sickness
Phenothiazines		
prochlorperazine (Compazine, Compro)	X	▪ Control of severe N/V ▪ Preoperative nausea control ▪ Treatment of N/V
promethazine (Phenergan)	X	▪ Treatment and prevention of N/V associated with motion sickness ▪ Prevention and control of N/V associated with certain types of anesthesia and surgery

Antiemetics Agents – Indications

Drugs	Generic	Indication(s)
NK1 receptor antagonists		
aprepitant capsules (Emend)	**X**	In combination with other antiemetic agents for: ▪ Acute and delayed nausea and vomiting (N/V) associated with highly emetogenic cancer chemotherapy (initial and repeat dosing), including high-dose cisplatin in patients ≥ 12 years old ▪ N/V associated with initial and repeat courses of moderately emetogenic cancer chemotherapy in patients ≥ 12 years old ▪ Prevention of post-operative N/V in adults Limitations of use: has not been studied for the treatment of established N/V; chronic continuous administration is not recommended
aprepitant injectable emulsion (Cinvanti)	**---**	In combination with other antiemetic agents for the prevention of: ▪ Acute and delayed N/V associated with initial and repeat courses of highly emetogenic cancer chemotherapy including high-dose cisplatin in adults ▪ N/V associated with initial and repeat courses of moderately emetogenic cancer chemotherapy in adults Limitation of use: has not been studied for treatment of established N/V
aprepitant suspension (Emend)	**---**	In combination with other antiemetic agents for: ▪ Acute and delayed N/V associated with highly emetogenic cancer chemotherapy (initial and repeat dosing), including high-dose cisplatin in patients ≥ 6 months old ▪ N/V associated with initial and repeat courses of moderately emetogenic cancer chemotherapy in patients ≥ 6 months old ▪ Prevention of post-operative N/V in adults Limitations of use: has not been studied for the treatment of established N/V; chronic continuous administration is not recommended
fosaprepitant (Emend for injection)	**---**	In combination with other antiemetic agents for: ▪ Prevention of acute and delayed N/V associated with initial and repeat courses of highly emetogenic cancer chemotherapy, including high-dose cisplatin in patients ≥ 6 months old ▪ Prevention of delayed N/V associated with initial and repeat courses of moderately emetogenic cancer chemotherapy in patients ≥ 6 months old Limitation of use: has not been studied for the treatment of established N/V
rolapitant (Varubi)	**---**	In combination with other antiemetic agents for: ▪ Prevention of acute and delayed N/V associated with initial and repeat courses of emetogenic cancer chemotherapy, including, but not limited to, highly emetogenic chemotherapy

Antiemetics Agents – Indications

Drugs	Generic	Indication(s)
5-HT3 Antagonists		
dolasetron (Anzemet)	---	▪ Prevention of N/V associated with moderately emetogenic cancer chemotherapy; including initial and repeat courses in adults and children ≥ 2 years of age ▪ Prevention of post-operative N/V in adults and children ≥ 2 years of age
granisetron	X	▪ Prevention of N/V associated with initial and repeat courses of emetogenic cancer therapy including high-dose cisplatin ▪ Prevention of N/V associated with radiation, including total body irradiation and fractionated abdominal radiation ▪ Injection: Prevention and treatment of post-operative N/V in adults
granisetron injection, extended-release (Sustol)	---	▪ In combination with other antiemetics in adults for the prevention of acute and delayed N/V associated in with initial and repeat courses of moderately emetogenic cancer chemotherapy or anthracycline and cyclophosphamide (AC) combination chemotherapy regimens
granisetron transdermal (Sancuso)	---	▪ Prevention of N/V in patients receiving moderately or highly emetogenic chemotherapy regimens of up to 5 consecutive days duration
ondansetron (Zofran)	X	▪ Prevention of N/V associated with initial and repeat courses of moderately emetogenic cancer chemotherapy ▪ Prevention of post-operative N/V
ondansetron soluble film (Zuplenz)	---	▪ Prevention of N/V associated with highly emetogenic cancer chemotherapy, including cisplatin ≥ 50 mg/m^2 ▪ Prevention of N/V associated with radiotherapy in patients receiving total body irradiation, single high-dose fraction to the abdomen, or daily fractions to the abdomen
palonosetron (Aloxi)	X	▪ Prevention of acute and delayed N/V associated with initial and repeat courses of moderately emetogenic cancer chemotherapy ▪ Prevention of acute N/V associated with initial and repeat courses of highly emetogenic cancer chemotherapy ▪ Prevention of post-operative N/V for up to 24 hours following surgery
Palonosetron	---	▪ Prevention of acute and delayed N/V associated with initial and repeat courses of moderately emetogenic cancer chemotherapy ▪ Prevention of acute N/V associated with initial and repeat courses of highly emetogenic cancer chemotherapy ▪ Prevention of post-operative N/V for up to 24 hours following surgery
palonosetron	---	▪ Prevention of acute and delayed N/V associated with initial and repeat courses of moderately emetogenic cancer chemotherapy in adults ▪ Prevention of acute N/V associated with initial and repeat courses of highly emetogenic cancer chemotherapy in adults

Antiemetics Agents – Indications

Drugs	Generic	Indication(s)
Combination (NK_1 + 5-HT_3 receptor antagonists) products		
fosnetupitant/palonosetron injectable (Akynzeo)	---	▪ In combination with dexamethasone in adults, for the prevention of acute and delayed N/V associated with initial and repeat courses of highly emetogenic chemotherapy *Limitation of use: fosnetupitant/palonosetron has not been studied for the prevention of N/V associated with anthracycline plus cyclophosphamide chemotherapy*
netupitant/palonosetron capsule (Akynzeo)	---	▪ In combination with dexamethasone in adults, for the prevention of acute and delayed N/V associated with initial and repeat courses of cancer chemotherapy, including, but not limited to, highly emetogenic chemotherapy
Cannabinoids		
dronabinol (Marinol)	**X**	▪ Treatment of N/V associated with cancer chemotherapy in patients who have failed to respond adequately to conventional antiemetic treatments ▪ Anorexia associated with weight loss in patients with AIDS
dronabinol (Syndros)	---	▪ Treatment of N/V associated with cancer chemotherapy in patients who have failed to respond adequately to conventional antiemetic treatments ▪ Anorexia associated with weight loss in patients with AIDS
nabilone (Cesamet)	---	▪ Treatment of N/V associated with cancer chemotherapy in patients who have failed to respond adequately to conventional antiemetic treatments
Antidopaminergic Agents		
metoclopramide oral disintegrating tablets (ODT)	**X**	▪ Relief of heartburn symptoms of refractory gastroesophageal reflux disease (GERD) when other treatments do not work ▪ Relief of symptoms of slow stomach emptying in patients with diabetes (diabetic gastroparesis)
metoclopramide (Reglan)	**X**	▪ Relief of symptoms associated with acute and recurrent diabetic gastroparesis ▪ Prevention of N/V associated with emetogenic cancer chemotherapy ▪ Prevention of post-operative N/V ▪ Small bowel intubation ▪ As short-term therapy for adults with symptomatic, documented gastroesophageal reflux (GERD) who fail to respond to conventional therapy
Antihistamines		
doxylamine/pyridoxine (Diclegis, Bonjesta)	---	▪ Treatment of N/V of pregnancy in women who do not respond to conservative management
Others		
phosphorated carbohydrate solution (Emetrol OTC)	**X**	▪ Relief of nausea due to upset stomach from intestinal flu, stomach flu, and food or drink indiscretions
trimethobenzamide (Tigan)	**X**	▪ Treatment of N/V associated with gastroenteritis

Treatment Guidelines- ASCO, 2017

- ASCO antiemetic guidelines recommend the choice of antiemetic treatment should be based on the radiotherapy and chemotherapy agent with the greatest degree of emetic risk
  - Optimal treatment should be used with initial chemotherapy to limit anticipatory nausea and vomiting
- Chemotherapy
  - Patients with minimal emesis risk should not be routinely offered antiemetic prophylaxis
  - For patients receiving low-emetic-risk chemotherapy, ASCO recommends adults should be offered a single dose of a 5-HT_3 antagonist or a single 8-mg dose of dexamethasone prior to treatment
  - For patients receiving moderately emetogenic chemotherapy (MEC), ASCO recommends treatment with a 2-drug combination of a 5-HT_3 antagonist and dexamethasone (day 1)
  - For patients who receive highly emetogenic chemotherapy (HEC), ASCO recommends a 4-drug combination of an NK1 receptor antagonist (duration based on formulation), a 5-HT3 receptor antagonist (day 1), dexamethasone (days 1 through 4), and olanzapine (days 1 through 4)
- Patients with breakthrough nausea and vomiting despite optimal prophylaxis, including olanzapine, may be offered an additional drug from another class for subsequent treatments (those who did not receive olanzapine should be offered olanzapine first)
- For multiday chemotherapy, after assessing emetic risk of the agents prescribed, patients should receive an agent of highest therapeutic index daily during chemotherapy and for 2 days thereafter

Treatment Guidelines- ASCO, 2017

- Radiation therapy
  - Patients with select low-emetogenic risk radiation therapy should be offered dexamethasone with other alternatives considered for rescue therapy based on prior treatment and location of radiation
  - Patients with moderately emetogenic radiation therapy should receive a 5-HT3 receptor antagonist with or without dexamethasone prior to each fraction for the first 5 fractions
  - Patients with highly emetogenic radiation therapy should receive a 5-HT_3 receptor antagonist and dexamethasone before each fraction and on the day after each fraction, even if radiation therapy is not planned for that day

- Pediatrics patients
  - Receiving MEC, ASCO recommends treatment with a 5-HT_3 receptor antagonist and dexamethasone
  - Receiving HEC, ASCO recommends treatment with a 5-HT_3 receptor antagonist, aprepitant (if eligible), and dexamethasone, noting that higher weight-based dosing may be necessary
    - Pediatric patients receiving HEC who are unable to receive dexamethasone should receive palonosetron and aprepitant

Treatment Guidelines- NCCN, 2019

- The choice of antiemetic should be based on emetic risk of the chemotherapy, prior experience with antiemetics, and patient factors. It should be initiated prior to the start of chemotherapy to provide maximal protection against chemotherapy-induced emesis
  - The antiemetic therapy should be continued for the same timeframe as the duration of the emetic activity of the chemotherapeutic agent being used

- The guidelines identify emesis prevention treatment options for high, moderate, low, and minimal emetic risk intravenous (IV) chemotherapy, oral chemotherapy, and radiation therapy, as well as breakthrough treatment for chemotherapy-induced N/V

- To prevent acute and delayed emesis, in patient receiving IV HEC
  - 3- or 4-drug combination of an NK1 receptor antagonist (duration and dosing is dependent on formulation), a 5-HT3 receptor antagonist (day 1), and dexamethasone (days 1 through 4), with or without olanzapine (days 1 through 4) or
  - 3-drug regimen of olanzapine, palonosetron, and dexamethasone may also be used

Treatment Guidelines- NCCN, 2019

- Prevent acute and delayed emesis in patient receiving IV MEC
  - 5-HT_3 antagonist and dexamethasone as a 3 day regimen
  - NK_1 antagonist should be added for select patients with additional risk factors or previous treatment failures with a steroid and 5-HT_3 antagonist alone (ranging from 1 to 3 days based on the treatment regimen selected)
  - NCCN does not specify one 5-HT_3 antagonist or NK_1 antagonist over another (or route/formulation)
  - Equivalent alternatives to this include 3-day olanzapine-containing regimens (olanzapine, palonosetron, and dexamethasone)

- For IV low emetogenic risk chemotherapy
  - Dexamethasone, metoclopramide (Reglan), prochlorperazine (Compazine, Compro), or an oral 5-HT_3 antagonist may be used and repeated daily for multiday doses of chemotherapy
  - There is no routine prophylaxis for patients who receive minimal emetic risk IV chemotherapy

- For breakthrough treatment of chemotherapy-induced N/V
  - The general principle is to add 1 agent from a different class, as needed, to the existing regimen (e.g., antipsychotic, benzodiazepine, cannabinoid, dopamine receptor antagonist, phenothiazine, 5-HT_3 antagonist, scopolamine patch, or corticosteroid)

- For radiation-induced N/V associated with upper abdomen/localized sites or total body irradiation
  - Oral granisetron or ondansetron with or without oral dexamethasone as pretreatment for each day of therapy

Treatment Guidelines- ASA, 2013

- The American Society of Anesthesiologists has published recommendations on the prevention of post-operative nausea and vomiting (PONV) within their guidelines on postanesthetic care
- They recommend routine assessment and monitoring for N/V
- For prophylaxis and treatment of N/V, they evaluated the following classes of medication and rated them based on the quality of evidence (range of A to C, from randomized controlled trials to informal opinion and determination of beneficial [B] or equivocal [E]):
    - Antihistamines (Category A3-B evidence)
    - 5-HT_3 receptor antagonists (Category A1-B evidence as a class)
    - Tranquilizers/neuroleptics (e.g., droperidol [Category A1-B evidence]
    - Haloperidol [Category A2-B evidence]
    - Hydroxyzine [Category A3-B evidence]
    - Perphenazine [Category A3-B evidence]
    - Prochlorperazine [Category A1-E evidence]
  - For prophylaxis of PONV using multiple agents, they determined that multiple agents may be used when needed (Category A2-B evidence)
  - They further note that pharmacologic treatment of N/V is recommended as it improves patient satisfaction and comfort and reduces time to discharge

Treatment Guidelines- ACOG, 2018

- Prompt treatment of N/V of pregnancy is important to prevent hyperemesis gravidarum
- First-line treatment of N/V of pregnancy consists of nonpharmacologic options (e.g., assessing supplementation change options, ginger capsules, acupressure)
- For persistent symptoms, pharmacologic treatment with vitamin B6 (pyridoxine) or vitamin B6 plus doxylamine, including co-formulated products such as Diclegis or Bonjesta, are recommended
  - If symptoms continue to persist, other medications can be considered for off-label use, including dimenhydrinate, diphenhydramine, prochlorperazine, and promethazine
  - Should symptoms continue to persist, treatment options are based on hydration status and include the previously mentioned off-label options as well as the additional options of chlorpromazine, methylprednisolone, metoclopramide, ondansetron, and trimethobenzamide
- No single method has demonstrated superiority over another and that treatment options within each step are presented alphabetically rather than in any preference order
- Diclegis, a fixed-dose combination of the antihistamine doxylamine 10 mg plus pyridoxine 10 mg, is the first FDA-approved, pregnancy category A delayed-release combination medication for the treatment of N/V of pregnancy

Magellan Rx MANAGEMENT℠

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Substance Use Disorder (Opiate Dependence)

Disease State Description – Opiate Dependence Treatments

- Prescription and illicit opioid abuse and misuse has reached national interest and was declared a National Public Health Emergency by the Department of Health and Human Services (DHHS) Acting Secretary in 2017
  - The 2017 National Survey on Drug Use and Health (NSDUH) reported there was an estimated 30.5 million Americans aged 12 years and older who were current (past month) illicit drug users
  - There were approximately 11.4 million people aged 12 or older in the United States (US) who misused opioids in the past year
  - Approximately 19.7 million people aged 12 or older in 2016 were considered to have a substance use disorder (SUD) in the past year, including 14.5 million people with an alcohol use disorder, 7.5 million people with an illicit drug use disorder, and 2.1 million had an opioid use disorder

- Drug Addiction Treatment Act of 2000 (DATA)
  - In order to become a qualified practitioner, physicians must be licensed under State law to practice medicine, obtain a waiver from the U.S. Substance Abuse and Mental Health Services Administration (SAMHSA), and notify the Secretary of Health and Human Services (HHS) of their intention of prescribing or dispensing buprenorphine
  - Such practitioners hold a modified Drug Enforcement Administration (DEA) registration, in which they are designated by a unique identifier and must include it on each prescription written
  - Prescribers are limited in the number of patients they may treat under a waiver, but they may request approval to treat additional patients

- Medication-assisted Treatment (MAT)
  - SAMHSA provides information on medication-assisted treatment (MAT), including training courses for buprenorphine use and opioid prescribing courses
  - They also provide guides for medication-assisted treatment of opioid use disorder that highlight contraindications, warnings, and other concerns and briefly address who ideal candidates would be for each medication; they do not state that any one medication is appropriate over another for all patients
  - The SAMHSA website provides additional information on medication-assisted treatment for providers and patients
  - Many of these resources are available to guide prescribers as they select a treatment option for both the induction and maintenance phases as well as assist in navigating the legal requirements related to the use of these medications where needed

Opiate Dependence Treatments – Indications

Drugs	Generic	Indication
buprenorphine sublingual tablets	X	▪ Treatment of opioid dependence (preferred for induction only); should be used as part of a complete treatment plan to include counseling and psychosocial support
buprenorphine extended-release injection (Sublocade)	---	▪ Treatment of moderate to severe opioid use disorder in patients who have initiated treatment with a transmucosal buprenorphine-containing product, followed by dose adjustment for a minimum of 7 days; should be used as part of a complete treatment plan that includes counseling and psychosocial support
buprenorphine implant (subdermal) (Probuphine)	---	▪ Maintenance treatment of opioid dependence in patients who have achieved and sustained prolonged clinical stability on low-to-moderate doses of a transmucosal buprenorphine containing product (e.g., doses of no more than 8 mg per day of Subutex or Suboxone sublingual tablet or generic equivalent); should be used as part of a complete treatment plan to include counseling and psychosocial support
buprenorphine/naloxone buccal film (Bunavail)	---	▪ Treatment of opioid dependence (induction and maintenance); should be used as part of a complete treatment plan to include counseling and psychosocial support
buprenorphine/naloxone sublingual film (Suboxone)	X	▪ Treatment of opioid dependence (induction and maintenance); should be used as part of a complete treatment plan to include counseling and psychosocial support
buprenorphine/naloxone sublingual tablets (Zubsolv)	---	▪ Treatment of opioid dependence (induction and maintenance); should be used as part of a complete treatment plan to include counseling and psychosocial support
buprenorphine/naloxone sublingual tablets	X	▪ Maintenance treatment of opioid dependence; should be used as part of a complete treatment plan to include counseling and psychosocial support
lofexidine (Lucemyra)	---	▪ Reduction of opioid withdrawal symptoms in adults following abrupt discontinuation of opioids
naloxone hydrochloride injection (Evzio)	---	▪ Emergency treatment of known or suspected opioid overdose, as manifested by respiratory and/or central nervous system depression; it is intended for immediate administration as emergency therapy in settings where opioids may be present
naloxone hydrochloride nasal spray (Narcan)	---	▪ Emergency treatment of known or suspected opioid overdose, as manifested by respiratory and/or central nervous system depression; it is intended for immediate administration as emergency therapy in settings where opioids may be present
naltrexone hydrochloride tablets	X	▪ Treatment of opioid dependence ▪ Treatment of alcohol dependence ▪ Naltrexone has not shown to provide any therapeutic benefit except as part of an appropriate plan of management for the addictions
naltrexone extended-release injectable suspension (Vivitrol)	---	▪ Prevention of relapse to opioid dependence, following opioid detoxification ▪ Treatment of alcohol dependence in patients who are able to abstain from alcohol in an outpatient setting ▪ Naltrexone ER injection should be part of a comprehensive management program that includes psychosocial support

Opioid Dependence Treatments – Guidelines

- **Risk Evaluation and Mitigation Strategies (REMS) Program**
  - There is a **buprenorphine-containing transmucosal products for opioid dependence (BTOD) REMS** that includes the following medications: buprenorphine tablets, buprenorphine/naloxone sublingual film and tablets, buprenorphine/naloxone sublingual tablets (Zubsolv), and buccal film (Bunavail)
    - Other elements in place to ensure safe buprenorphine and buprenorphine/naloxone product use include verification of safe use conditions and patient monitoring
  - Buprenorphine extended-release injection (**Sublocade**) has a REMS program to ensure the healthcare setting and pharmacy is certified and that the injection is dispensed directly from the pharmacy to a healthcare provider to avoid the risk of serious harm or death due to intravenous administration
  - There is also a shared REMS for **Suboxone** and **Subutex** branded products; however, only the Suboxone (buprenorphine/naloxone) film remains available and the branded tablets have been discontinued
  - Buprenorphine implant (**Probuphine**) also has its own REMS program
    - The buprenorphine implant has select requirements for both prescribers and for surgeons who implant or remove the insert to further ensure safety of use
  - **Naltrexone** ER injectable suspension (Vivitrol) also has a REMS program consisting of a medication guide and a communication plan
  - Ultimately, the goal of these REMS is to mitigate the risk of overdose, abuse, and misuse
    - Each includes a medication guide, an implementation system, and elements to ensure safe use
    - The REMS program consists of enrollment by the wholesaler, healthcare setting, and pharmacy to control distribution and administration

Opioid Dependence Treatments – Guidelines

- American Society of Addiction Medicine (ASAM), 2015
  - Published guidelines for the use of medications in the treatment of addiction involving opioid use
  - State that the choice of medication (e.g., buprenorphine, methadone, naltrexone) should be a shared decision between the clinician and patient and should consider patient preferences, treatment history, and treatment setting
  - Buprenorphine and methadone are the standard treatment options for managing the acute withdrawal from opioids
    - Buprenorphine may not be appropriate for patients with an active alcohol disorder or sedative-drug disorder
    - Methadone is recommended for patients who may benefit from additional supervision
  - Oral naltrexone requires special attention to medication adherence and may require observed administration for some patients
  - Lofexidine (Lucemyra) is the only FDA-approved non-opioid treatment for the management of opioid withdrawal symptoms
  - In 2017, ASAM adopted guidance on the appropriateness of drug testing to guide clinicians in the clinical setting and emphasizes that the frequency and duration of testing should be individualized
  - Acute symptoms are typically managed in an inpatient setting for close monitoring
    - Alpha$_2$ adrenergic agonists are often used in combination with other agents to target multiple withdrawal symptoms
    - Following the acute withdrawal period, there is no consensus on the ideal duration of maintenance therapy, despite the availability of multiple guidelines and resources for the initiation and management of medications for opioid dependency

Opioid Dependence Treatments – Guidelines

- Centers for Disease Control and Prevention (CDC), 2016
  - Guidelines for prescribing opioids for chronic pain outside of active cancer, palliative, and end-of-life care
  - These guidelines are intended to encourage appropriate opioid use and help curb the opioid epidemic
  - Regarding medications for opioid dependence, the CDC states prescribers should offer treatment for opioid use disorder (e.g., medication-assisted treatment, such as buprenorphine or methadone, in combination with behavioral therapies)
  - Buprenorphine and methadone may be used in pregnant patients, but they state that oral or long-acting injectable formulations should be reserved for nonpregnant adults and those who are highly motivated
  - **The CDC released an updated statement in 2019 regarding the intent of the 2016 guidelines to advise primary care providers treating adults with certain types of chronic pain**
    - **The recommendations emphasize the careful tapering of opioids to avoid withdrawal symptoms in current pain patients and individualized assessment of risks and benefits for continued high-dose treatment**

- Surgeon General of the United States, 2018
  - Issued an advisory Surgeon General's Advisory on Naloxone and Opioid Overdose
  - In support to access naloxone for patients, health care practitioners, family and friends, and community members who may come into contact with patients on prescription high-dose opioids, illicit heroin or fentanyl, or patients with opioid use disorder

- World Health Organization (WHO), 2014
  - Has published guidelines on the identification and management of substance use disorders in pregnancy
  - State pregnant women should be encouraged to use opioid maintenance treatment whenever available rather than attempt opioid detoxification (strong recommendation, very low quality of evidence) and patients should be advised to either continue or initiate treatment with buprenorphine or methadone (strong recommendation, very low quality of evidence)

Opiate Dependence Treatments – Guidelines

- US Department of Health and Human Services (DHHS), 2018
  - Recommend clinicians co-prescribe naloxone to patients prescribed an opioid who are at risk of opioid overdose
    - This includes patients receiving ≥ 50 morphine milligram equivalents (MME) per day, with respiratory illness, receiving a benzodiazepine, or with a concomitant non-opioid substance use disorder (e.g., alcohol)
    - Naloxone should also be prescribed to individuals at a high risk of experiencing or responding to an opioid overdose, such as a family member or friend of a person with an opioid use disorder, including those who have decreased opioid tolerance (e.g., after release from incarceration or other controlled setting)

- U.S. Food and Drug Administration (FDA), 2016
  - In response to the opioid abuse epidemic, in April 2016, the FDA announced plans to reassess their approach to opioid medications with a focus on policies to reverse the epidemic of deaths associated with opioid use
  - Plans include the use of an expert advisory committee prior to the approval of an opioid without abuse-deterrent properties, the formation of a Pediatric Advisory Committee who will review pediatric labeling for new products, an update of Risk Evaluation and Mitigation Strategies (REMS) requirements, and improvement in access to abuse-deterrent formulations, naloxone, and other treatment options for patients with opioid-use disorders
  - **In addition to the CDC and FDA advisory committees focus on the opioid epidemic, the FDA has also awarded a contract to the National Academies of Sciences, Engineering, and Medicine (NASEM) to develop evidence-based guidelines for opioid prescribing in specific acute pain conditions**
    - **The goal of this program is to decrease inappropriate opioid prescribing that may lead to excess opioid supply and inappropriate exposure while maintaining access to adequate pain control for patients**

Magellan Rx MANAGEMENT℠

Magellan Medicaid Administration

Prostatic Hypertrophy Agents (BPH Agents)

Disease State Description – Benign Prostatic Hyperplasia

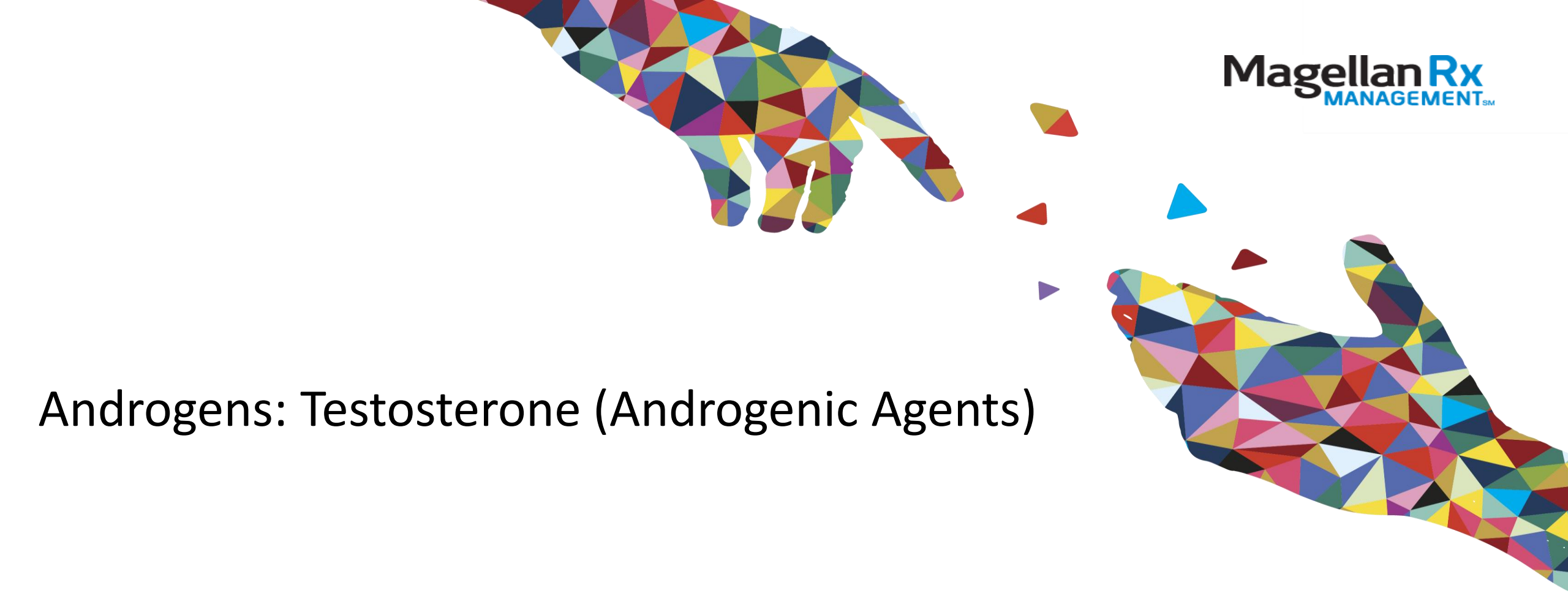
- **Benign prostatic hyperplasia (BPH)**
  - One of the most common conditions in aging men
  - ~14 million men in the United States have symptoms related to BPH
    - ~50% of men demonstrate histopathologic BPH by age 60 years
    - This number increases to 90% by 85 years of age
  - The symptoms of BPH are induced by hyperplastic changes in prostate tissue, leading to prostatic enlargement
  - The resulting obstruction increases urinary outflow resistance and results in an impaired detrusor muscle response
  - Although prostatic enlargement is mediated by epithelial and smooth muscle cells, the etiology of initial hyperplastic changes is currently unknown
- Patients with BPH may present with bothersome lower urinary tract symptoms (LUTS) resulting from irritation (urinary frequency, nocturia, urgency, urge incontinence) and/or obstruction (difficulty initiating urination or passing urine, weak stream, involuntary postvoid dripping of urine, and sensation of incomplete bladder emptying)
- Most men with BPH experience only mild or moderate symptoms of obstruction
- Severe BPH, more likely to occur in men over 60 years of age, can lead to urinary retention, renal insufficiency, urinary tract infections, hematuria, and bladder stones
  - More serious complications, such as uremia and irreversible bladder dysfunction, are uncommon

Benign Prostatic Hyperplasia – Indications

Drugs	Generic	HTN	BPH
Alpha-Blockers			
alfuzosin ER (Uroxatral)	X		X
doxazosin (Cardura)	X	X	X
doxazosin ER (Cardura XL)	---		X
silodosin (Rapaflo)	X		X
tamsulosin (Flomax)	X		X
terazosin	X	X	X
5-Alpha Reductase (5AR) Inhibitors			
dutasteride (Avodart)	X		▪ Treatment of symptomatic BPH in men with enlarged prostate to improve symptoms, reduce the risk of acute urinary retention, and reduce the risk of the need for BPH-related surgery ▪ Treatment of symptomatic BPH in combination with the alpha-blocker, tamsulosin, in men with an enlarged prostate ▪ Limitations of use: Not approved for the prevention of prostate cancer
finasteride (Proscar)	X		▪ Treatment of symptomatic BPH in men with enlarged prostate to improve symptoms, reduce the risk of acute urinary retention, and reduce the risk of the need for BPH-related surgery including transurethral resection of the prostate (TURP) or prostatectomy ▪ Treatment of symptomatic BPH in combination with the alpha-blocker, doxazosin, to reduce the risk of symptomatic progression of BPH ▪ Limitations of use: Not approved for the prevention of prostate cancer
5-Alpha Reductase (5AR) Inhibitors / Alpha-Blocker Combinations			
dutasteride/tamsulosin (Jalyn)	X		▪ Treatment of symptomatic BPH in men with enlarged prostate ▪ Limitations of use: Not approved for the prevention of prostate cancer
Phosphodiesterase 5 (PDE5) Inhibitors			
tadalafil (Cialis)	X		▪ Treatment of signs and symptoms of BPH ▪ Note: tadalafil is also indicated for the treatment of erectile dysfunction, with or without BPH; this indication will not be included in this review ▪ Limitations of use: If tadalafil is used with finasteride to begin BPH treatment, its use is recommended for up to 26 weeks; ▪ The incremental benefit of tadalafil decreases from 4 weeks until 26 weeks, and the incremental benefit of tadalafil beyond 26 weeks is unknown

Disease State Description – Benign Prostatic Hyperplasia

- American Urological Association (AUA) 2010 standards (reaffirmed in 2014)
  - Patients with mild symptoms of BPH (AUA Symptom Score < 8) and patients with moderate or severe symptoms (AUA Symptom Score > 8) who are not bothered by their symptoms (e.g., they do not interfere with the daily activities of living) should be managed using a strategy of watchful waiting
  - Alpha-adrenergic blocker therapy is an appropriate treatment option for patients with moderate to severe LUTS secondary to BPH
  - The guidelines state that alfuzosin (Uroxatral), doxazosin (Cardura), tamsulosin (Flomax), and terazosin are appropriate treatment options for patients with LUTS secondary to BPH
    - Although there are slight differences in the adverse event profiles of these agents, the AUA states that all 4 agents have equal clinical effectiveness
    - Silodosin (Rapaflo) did not have published peer-reviewed studies prior to the deadline for literature evaluation for the guideline update
  - The guidelines also state that the 5α-reductase inhibitors, finasteride (Proscar) and dutasteride (Avodart), are appropriate and effective treatments for patients with LUTS associated with demonstrable prostatic enlargement, but they are not appropriate treatments for men with LUTS who do not have evidence of prostatic enlargement
    - The 5α-reductase inhibitors may be used to prevent progression of LUTS secondary to BPH and to reduce the risk of urinary retention and future prostate-related surgery
    - The patient should also be advised of the disadvantages of this therapeutic approach (e.g., side effects such as sexual dysfunction) and the need for long-term daily therapy in comparison to a reasonable estimate of his baseline risk of progression (e.g., retention and the risks associated with BPH-related surgery) so an informed decision may be made
  - Combination therapy utilizing an α-adrenergic receptor blocker and a 5α-reductase inhibitor presents an appropriate and effective treatment for patients who not only exhibit LUTS symptoms, but also have definitive prostatic enlargement



Androgens: Testosterone (Androgenic Agents)

Magellan Medicaid Administration

Overview of Disease State

- Male hypogonadism is caused by insufficient production of testosterone and characterized by low serum concentrations and may present as testosterone deficiency, infertility, or both
- Approximately 20% of men ages 60 to 69 years old and 30% of men ages 70 to 79 years old have serum testosterone levels below the normal range
- Symptoms at presentation will primarily depend on the patient's age at the time of disease onset and can include
  - Impotence
  - Decreased libido
  - Fatigue
  - Loss of energy
  - Mood Depression
  - Regression of secondary sex characteristics
- Potential risks due to male hypogonadism include
  - Osteoporosis
  - Sexual dysfunction
  - Depression
  - Cardiovascular disease

Androgenic Agents - Indications

Drugs	Generic	FDA-Approved Indications
testosterone gel (AndroGel)	X	Testosterone replacement therapy in males for conditions associated with a deficiency or absence of endogenous testosterone, such as primary or secondary hypogonadism (congenital or acquired)
testosterone gel (Fortesta)	X	
testosterone gel (Testim)	X	
testosterone gel (Vogelxo)	X	
testosterone nasal gel (Natesto)	---	
testosterone solution (Axiron)	X	
testosterone transdermal system (Androderm)	---	

Androgenic Agents - Dosing and Availability

Drugs	Generic	Dosing	Administration	Availability
testosterone 1% gel (Androgel 1%)	X	5 g daily, preferably in the morning (delivers 5 mg systemically) Dosing may be increased to 10 mg (by 2.5 mg increments)	Apply to clean, dry, intact skin of the shoulders and upper arms Do not apply to the genitals	2.5, 5 g packets (contains 25 mg or 50 mg testosterone, respectively; 30 packets) 75 g pump with 60 pump actuations delivering 12.5 mg of testosterone per actuation (1.25 g of gel)
testosterone 1.62% gel (Androgel 1.62%)	X	40.5 mg (1.25 g of gel) once daily Dosing may be adjusted between 20.25 mg and 81 mg based on levels drawn at 14 and 28 days after start of therapy	Apply to clean, dry, intact skin of the shoulders and upper arms Do not apply to the genitals	1.25, 2.5 g packets (contains 20.25 mg or 40.5 mg testosterone, respectively; 30 packets) 75 g pump with 60 pump actuations delivering 20.25 mg of testosterone per actuation (1.25 g of gel)
testosterone gel (Fortesta)	X	Initiate at 40 mg once every morning Dosing may be adjusted from 10 mg to 70 mg based on levels 2 hours after application at days 14 and 35 after start of last adjustment	Apply to clean, dry, intact skin of the front and inner thighs Do not apply to genitals or other parts of the body	In a 60 g canister with metered dose pump delivering 10 mg testosterone in 0.5 g gel per actuation
testosterone gel (Testim)	X	5 g daily, preferably in the morning (delivers 5 mg systemically)	Apply to clean, dry, intact skin of the shoulders and/or upper arms Do not apply to genitals or abdomen	5 g tubes (30 per package)

Androgenic Agents - Dosing and Availability

Drugs	Generic	Dosing	Administration	Availability
testosterone gel (Vogelxo)	X	50 mg applied topically once daily at approximately the same time each day Dosing may be adjusted to 100 mg once daily based on levels drawn at 14 days after start of therapy; Maximum dose is 100 mg daily	Apply to clean, dry, intact skin of the shoulders and/or upper arms Do not apply to genitals or abdomen	In unit-dose tubes or packets containing 50 mg testosterone in 5 g of gel; multiple-dose metered pumps delivering 12.5 mg of testosterone in 1.25 g of gel per actuation
testosterone nasal gel (Natesto)		11 mg total, or 1 pump actuation in each nostril, 3 times a day (once in the morning, once in the afternoon, and once in the evening, about 6 to 8 hours apart) Maximum total daily dose is 33 mg intranasally	Patients should blow nose prior to administration Actuator should be tipped toward lateral wall of nostril to ensure gel is applied appropriately prior to pressing the pump Refrain from blowing nose or sniffing for 1 hour following administration Do not apply to genitals or abdomen	Metered dose pump containing 11 g of gel dispensed as 60 metered pump actuations; each actuation delivers 5.5 mg of testosterone
testosterone solution (Axiron)	X	Initiate at 60 mg once a day Dosing may be adjusted 30 mg based on levels drawn 2 to 8 hours after application at days 14 after start or last adjustment	Apply to clean, dry, intact skin of the axilla preferably at the same time every morning Do not apply to the genitals or other parts of the body	110 mL of topical solution in a metered dose pump; each pump delivers 30 mg of testosterone in 1.5 mL of solution; each bottle has an applicator top
testosterone transdermal system (Androderm)		4 mg daily (nightly)	Apply to clean, dry skin of the back, abdomen, upper arms, or thighs; do not apply to genitals, bony prominences, or parts of the body that may be subject to prolonged pressure due to sitting or sleeping; rotate sites every 7 days	2 mg patches (60 per carton); 4 mg patches (30 per carton) Patches contain 9.7 mg testosterone (delivering 2 mg/day) or 19.5 mg (delivering 4 mg/day)

Androgenic Agents - Dosing and Availability

Drugs	Indication(s)	Dosing	Availability
oxymetholone (Anadrol-50)	• Acquired aplastic anemia • Anemia of chronic renal failure • Antineoplastic adverse reaction Myelosuppression • Fanconi's anemia • Pure red cell aplasia	• 1 to 5 mg/kg orally daily	Oral Tablets: 50 mg
methyltestosterone (Methitest)	• Delay in sexual development AND/OR puberty, Male • Hypogonadotropic hypogonadism • Metastasis from malignant tumor of breast, inoperable metastatic disease (skeletal) in women 1 to 5 years postmenopausal • Primary hypogonadism	**Delay in sexual development AND/OR puberty, Male** • 10 to 50 mg orally daily for 4 to 6 months **Hypogonadotropic hypogonadism** • 10 to 50 mg orally daily **Metastasis from malignant tumor of breast, inoperable metastatic disease (skeletal) in women 1 to 5 years postmenopausal** • 50 to 200 mg orally daily **Primary hypogonadism** • 10 to 50 mg orally daily	Oral Capsule: 10 mg
oxandrolone (Oxandrin)	• Adjunctive therapy to promote weight gain after weight loss following extensive surgery, chronic infections, or severe trauma, and in some patients who without definite pathophysiologic reasons fail to gain or to maintain normal weight	• 2.5 to 20 mg orally per day in 2 to 4 divided doses • Duration of 2 to 4 weeks is usually adequate, depending on clinical response and tolerance	• Oral Tablets: 2.5, 10 mg
testosterone buccal system (Striant)	• Replacement therapy in males for conditions associated with a deficiency or absence of endogenous testosterone	• Application of one buccal system (30 mg) to the gum region twice daily • Morning and evening (about 12 hours apart) • Striant should be placed in a comfortable position just above the incisor tooth (on either side of the mouth) • With each application, Striant should be rotated to alternate sides of the mouth.	• Buccal Patch, Extended Release: 30 mg

Androgenic Agents – Guideline

- Endocrine Society (ES), 2018 - treatment guidelines for hypogonadism
  - The guidelines recommend
    - A diagnosis of hypogonadism be made only if the patient has symptoms of testosterone deficiency and clearly and consistently low serum testosterone (T) levels, typically based on repeated fasting morning total T levels
      - Additional diagnostic evaluation should be performed to determine the cause of androgen deficiency
    - Against testosterone therapy without further urological evaluation in patients with palpable prostate nodule or induration or prostate specific antigen (PSA) 4 ng/mL or PSA 3 ng/mL in men at high risk of prostate cancer, such as African Americans or men with first-degree relatives with prostate cancer
    - Against testosterone treatment in patients with hematocrit > 48%, untreated severe obstructive sleep apnea, severe lower urinary tract symptoms associated with benign prostatic hypertrophy, and uncontrolled or poorly controlled congestive heart failure
  - Testosterone treatment is aimed at inducing and maintaining secondary sex characteristics and at improving their sexual function, sense of well-being, and bone mineral density
    - Treatment goals are continuation of normal activities of daily living and decreased risk of secondary complications such as infertility, osteoporosis, fatigue, and mood disturbances
    - Target testosterone levels while on therapy should be in the mid-normal range
    - Monitor serum testosterone, hematocrit, and prostate cancer risk during the first year of treatment
  - Use of testosterone in men ages ≥ 65 years is not recommended due to unclear risk versus benefit profile in this population
    - ES also recommends against testosterone therapy in men who are planning fertility in the near future or in patients with breast or prostate cancer
  - While ES provides advantages and disadvantages of each formulations, no preference of any testosterone replacement product is provided
    - Choice of formulations should be based on patient preference and drug pharmacokinetics, adverse effect profile, treatment burden, and cost
  - Testosterone transfer to another person who is in close contact as a potential adverse event for the transdermal gel formulations

Androgenic Agents – Guideline

- American Urological Association (AUA), 2018
  - Provides a treatment algorithm for evaluating and managing testosterone deficiency
  - The AUA recommends a total T level < 300 ng/dL based on 2 early morning tests taken on 2 different days to support a diagnosis of low testosterone in symptomatic males
  - Adjunctive testing (serum luteinizing hormone, serum prolactin, serum estradiol, hemoglobin, hematocrit, PSA) may be considered
  - Measuring total T level is recommended in patients with a history of unexplained anemia, bone density loss, HIV/AIDS, chronic narcotic use, male infertility, pituitary dysfunction, chronic corticosteroids use, and exposure to chemotherapy or testicular radiation
  - In patients who are candidates for testosterone deficiency, they recommend a cardiovascular (CV) disease risk assessment be performed and patients at high risk for a CV event should be referred for further evaluation
  - Topical and injectable formulations can be considered without preference of 1 product over another

Appendices

Antipsychotics – Dosing & Availability

Drug	Schizophrenia/Psychotic Disorders		Other Indication	Dosage Forms
	Initial Dose	Usual Maintenance Dose		
First Generation Antipsychotics				
amitriptyline/ perphenazine	25/2 mg to 50/8 mg 3 to 4 times daily	Stable dose 2 to 4 times daily	--	Tablets: 10/2 mg, 10/4 mg, 25/2 mg, 25/4 mg, 50/4 mg
chlorpromazine	Oral: 25 mg 3 times daily IM: ≤ 25 mg x 1 dose, may repeat as 25 mg to 50 mg as needed hourly	Oral: up to 1,000 mg daily IM: 300 mg to 800 mg per day (divided) every 4 to 6 hours	Oral: 25 to 100 mg 3 or 4 times daily IM: 12.5 to 50 mg every 3-8 hours	Tablets: 10 mg, 25 mg, 50 mg, 100 mg, 200 mg Vials for injection: 25 mg/mL
fluphenazine	Oral: 2.5 mg to 10 mg 3 to 4 times daily IM (hydrochloride): 1.35 mg every 6 to 8 hours IM/SC (decanoate): 12.5 mg to 25 mg, injection may control symptoms for 4 to 6 weeks	Oral: 1 mg to 5 mg daily IM (hydrochloride): 2.5 mg to 10 mg per day (divided) every 6 to 8 hours IM/SC (decanoate): 50 mg every 1 to 4 weeks as needed/tolerated	--	Tablets: 1 mg, 2.5 mg, 5 mg, 10 mg Elixir: 2.5 mg/5 mL Concentrate: 5 mg/mL Vials for injection: 2.5 mg/mL (hydrochloride), 125 mg/5 mL (decanoate)
haloperidol (Haldol)	Oral: 0.5 mg to 2 mg 2 to 3 times daily IM (lactate): 2 mg to 5 mg every 4 to 8 hours (up to every 1 hour; maximum dose: 20 mg/day IM (decanoate): 10 to 15 times the oral daily dose, generally every 4 weeks (maximum: 450 mg/month)	Up to 100 mg daily for tablets and elixir; 20 mg daily for lactate injection; 450 mg per month for decanoate	0.5 to 1.5 mg 3 times daily (Tourette's); 0.05 to 0.075 mg/kg/day (behavioral disorders, hyperactivity)	Tablets†: 0.5 mg, 1 mg, 2 mg, 5 mg, 10 mg, 20 mg Elixir/concentrate†: 2 mg/mL Ampules/vials/syringe for injection: 5 mg/mL (lactate); Ampules/vials for injection 50 mg/mL, 100 mg/mL (decanoate)
loxapine	10 mg twice daily	60 mg to 100 mg divided into 2 to 4 doses daily	--	Capsules: 5 mg, 10 mg, 25 mg, 50 mg
loxapine inhalation powder (Adasuve)	Oral inhalation: 10 mg; only 1 dose should be administered within a 24-hour period			Single-use inhaler: 10 mg
molindone	50 mg to 75 mg in 3 to 4 divided doses	5 mg to 25 mg 3 to 4 times daily, up to 225 mg daily	--	Tablets: 5 mg, 10 mg, 25 mg
perphenazine	4 mg to 8 mg 3 times daily	Up to 64 mg daily	--	Tablets: 2 mg, 4 mg, 8 mg, 16 mg
pimozide (Orap)	--	--	0.2 mg/kg/day for Tourette's	Tablets: 1 mg, 2 mg
thioridazine	50 mg to 100 mg 3 times daily	Up to 800 mg daily	--	Tablets: 10 mg, 25 mg, 50 mg, 100 mg
thiothixene	2 mg 3 times daily	Up to 60 mg daily	--	Capsules: 1 mg, 2 mg, 5 mg, 10 mg
trifluoperazine	2 mg to 5 mg twice daily	15 mg to 20 mg daily	1 to 2 mg twice daily (non-psychotic anxiety)	Tablets: 1 mg, 2 mg, 5 mg, 10 mg

Antipsychotics – Dosing & Availability

Drug	Other Indications	Schizophrenia		Bipolar Disease		Dosage Forms
		Initial Dose	Maintenance Dose	Initial Dose	Maintenance Dose	
Second Generation Antipsychotics						
aripiprazole (Abilify, Abilify Maintena; Abilify Mycite)	Adjunctive treatment for depression: 2 mg to 5 mg daily, maintenance dose 5 mg to 10 mg daily (maximum dose: 15 mg daily) Tourette's disorder: < 50 kg: initial dose 2 mg daily, maintenance dose 5 mg daily (maximum dose 10 mg daily) > 50 kg: initial dose 2 mg daily, maintenance dose 10 mg daily (maximum dose 20 mg daily)	Oral: 10 mg to 15 mg once daily IM: 9.75 mg (maximum dose = 30 mg daily) IM (Maintena): 400 mg monthly	10 mg to 15 mg once daily (maximum dose = 30 mg daily) IM (Maintena): 400 mg IM once monthly based upon tolerability	15 mg once daily IM: 9.75 mg (maximum dose = 30 mg daily) 10 mg to 15 mg once daily (adjunct to lithium and valproate)	15 mg once daily Maximum dose = 30 mg/day IM (Maintena): 400 mg monthly	Tablets: 2 mg, 5 mg, 10 mg, 15 mg, 20 mg, 30 mg Orally disintegrating tablets: 10 mg, 15 mg Oral solution: 1 mg/mL Mycite tablets with sensor kit‡: 2 mg, 5 mg, 10 mg, 15 mg, 20 mg, 30 mg Maintena extended-release suspension in syringes and lyophilized powder in vials for injection: 300 mg and 400 mg and suspension
aripiprazole lauroxil ER (Aristada)	--	441 mg, 662 mg, or 882 mg monthly, 882 mg every 6 weeks, or 1,064 mg every 2 months	441 mg, 662 mg, or 882 mg monthly, 882 mg every 6 weeks, or 1,064 mg every 2 months	--	--	Extended-release suspension for injection in syringes: 441 mg/1.6 mL, 662 mg/2.4 mL, 882 mg/3.2 mL, 1,064 mg/3.9 mL
aripiprazole lauroxil ER (Aristada Initio)	--	One 675 mg dose (plus a single oral aripiprazole 30 mg dose in conjunction with the first Aristada injection); it is not intended for repeat dosing	--	--	--	Extended-release suspension for injection in syringe: 675 mg/2.4 mL
asenapine (Saphris)	--	Acute: 5 mg twice daily Maintenance: 5 mg twice daily	Acute: 5 mg twice daily Maximum dose = 10 mg twice daily Maintenance: 10 mg twice daily Maximum dose = 10 mg twice daily	Acute: 10 mg twice daily as monotherapy 5 mg twice daily (adjunct to lithium and valproate)	5 mg to 10 mg twice daily Maximum dose = 10 mg twice daily 5 mg to 10 mg twice daily (adjunct to lithium and valproate or monotherapy) Maximum dose = 10 mg twice daily	Sublingual tablets: 2.5 mg, 5 mg, 10 mg (black cherry flavor)

Antipsychotics – Dosing & Availability

Drug	Other Indications	Schizophrenia		Bipolar Disease		Dosage Forms
		Initial Dose	Maintenance Dose	Initial Dose	Maintenance Dose	
Second Generation Antipsychotics						
brexpiprazole (Rexulti)	Adjunctive treatment of major depressive disorder: starting 0.5 mg or 1 mg once daily, target dose 2 mg once daily, maximum 3 mg daily	1 mg once daily on Days 1 to 4	2 mg to 4 mg once daily Maximum dose = 4 mg daily	--	--	Tablets: 0.25 mg, 0.5 mg, 1 mg, 2 mg, 3 mg, 4 mg
cariprazine (Vraylar)	--	1.5 mg once daily; may be increased to 3 mg by Day 2	1.5 mg to 6 mg once daily	1.5 mg once daily; may be increased to 3 mg by Day 2	3 mg to 6 mg once daily	Capsules: 1.5 mg, 3 mg, 4.5 mg, 6 mg Titration pack: one 1.5 mg and six 3 mg capsules
clozapine (Clozaril)	--	12.5 mg once or twice daily	Target: 300 to 450 mg/day Maximum dose= 900 mg/day	--	--	Tablets: 25 mg, 50 mg†, 100 mg, 200 mg
clozapine (Fazaclo)						ODT: 12.5 mg, 25 mg, 100 mg, 150 mg, 200 mg
clozapine (Versacloz)						Suspension: 50 mg/mL
iloperidone (Fanapt)	--	1 mg twice daily	12 mg to 24 mg twice daily	--	--	Tablets: 1 mg, 2 mg, 4 mg, 6 mg, 8 mg, 10 mg, 12 mg Titration pack: 8 tablets with 2 tablets each of 1 mg, 2 mg, 4 mg, and 6 mg
lurasidone (Latuda)	--	40 mg once daily with food	40 mg to 160 mg once daily with food Maximum dose = 160 mg/day	20 mg once daily with food	20 mg to 120 mg once daily with food Maximum dose = 160 mg/day	Tablets: 20 mg, 40 mg, 60 mg, 80 mg, 120 mg
olanzapine (Zyprexa, Zyprexa Relprevv)	--	5 mg to 10 mg once daily IM (short-acting): 2.5 mg to 10 mg IM (long-acting): 150 mg to 300 mg every 2 weeks or 405 mg every 4 weeks	10 mg once daily IM (short-acting): up to 30 mg daily IM (long-acting): after 8 weeks, 150 mg to 300 mg every 2 weeks or 300 mg to 405 mg every 4 weeks	Manic or mixed: 10 mg to 15 mg once daily IM (short-acting): 2.5 mg to 10 mg	Manic or mixed: 5 mg to 20 mg once daily IM (short-acting): Up to 30 mg daily	Tablets: 2.5 mg, 5 mg, 7.5 mg, 10 mg, 15 mg, 20 mg ODT: 5 mg, 10 mg, 15 mg, 20 mg Immediate release vial for injection: 10 mg Relprevv extended-release vial for injection and as a kit containing diluent and syringes: 210 mg, 300 mg, 405 mg
olanzapine/ fluoxetine (Symbyax)	Treatment-resistant depression: 6/25 mg daily in evening	--	--	6/25 mg daily in evening	6/25 mg to 12/50 mg daily in evening	Capsules: 3/25 mg, 6/25 mg, 6/50 mg, 12/25 mg§, 12/50 mg

Antipsychotics – Dosing & Availability

Drug	Other Indications	Schizophrenia		Bipolar Disease		Dosage Forms
		Initial Dose	Maintenance Dose	Initial Dose	Maintenance Dose	
Second Generation Antipsychotics						
paliperidone ER (Invega) **paliperidone palmitate (Invega Sustenna, Invega Trinza)**	Schizoaffective disorder: initial 6 mg/day, maintenance 3 to 12 mg/day (maximum 12 mg/day) IM (Invega Sustenna): initial 234 mg/day on day 1 then 156 mg/day on day 8, maintenance 78 to 234 mg/day (maximum 234 mg/day)	6 mg once daily Invega Sustenna IM: 234 mg IM on day 1, then 156 mg IM 1 week later IM (Invega Trinza): once every 3 months; dose dependent upon previous dose of Invega Sustenna	3 mg to 12 mg once daily (maximum dose = 12mg/day) Invega Sustenna IM: 117 mg monthly (range 39 mg to 234 mg)	--	--	Tablets: 1.5 mg, 3 mg, 6 mg, 9 mg Sustenna extended-release injection: 39 mg, 78 mg, 117 mg, 156 mg, 234 mg Trinza extended-release injection: 273 mg, 410 mg, 546 mg, 819 mg
pimavanserin (Nuplazid)	Psychosis associated with Parkinson's disease: 34 mg once daily	--	--	--	--	Tablets: 10 mg, 17 mg Capsule: 34 mg
quetiapine Seroquel)	Bipolar depression Initial 50 mg/day, maintenance 300 mg/day, maximum 300 mg/day	25 mg twice daily	150 to 750 mg/day; divided into 2 to 3 doses	50 mg twice daily	400 to 800 mg/day	Tablets: 25 mg, 50 mg, 100 mg, 200 mg, 300 mg, 400 mg
quetiapine ER (Seroquel XR)	Major depressive disorder in combination with antidepressants: initial 50 mg/day, recommended 150 to 300 mg/day Depressive episodes associated with bipolar disorder: initial 100 mg/day, recommended 300 mg/day	300 mg in the evening	400 to 800 mg/day	300 mg in the evening	400 to 800 mg/day	ER tablets: 50 mg, 150 mg, 200 mg, 300 mg, 400 mg
risperidone Perseris)	--	90 mg or 120 mg SC once monthly	90 mg or 120 mg SC once monthly	--	--	ER injection: 90 mg, 120 mg
risperidone (Risperdal, Risperdal Consta)	--	2 mg/day (in 1 to 2 divided doses) IM (Risperdal Consta): 25 mg every 2 weeks	4 to 8 mg/day (range, 4 to 16 mg/day) IM (Risperdal Consta): 25 mg to 50 mg every 2 weeks	2 mg to 3 mg once daily IM (Risperdal Consta): 25 mg every 2 weeks	1 to 6 mg/day IM (Risperdal Consta): 25 mg to 50 mg every 2 weeks	Tablets: 0.25 mg, 0.5 mg, 1 mg, 2 mg, 3 mg, 4 mg ODT: 0.25, 0.5, 1, 2, 3, 4 mg Oral solution: 1 mg/mL Consta ER injection: 12.5, 25, 37.5, 50 mg
ziprasidone (Geodon)	--	20 mg twice IM: 10 to 20 mg	40 mg to 80 mg twice daily IM: Up to 40 mg daily for 3 consecutive days	40 mg twice daily	40 mg to 80 mg twice daily	Capsules: 20 mg, 40 mg, 60 mg, 80 mg Vial: 20 mg

Antipsychotics – Dosing & Availability (Pediatrics)

Drug	Other Indications	Schizophrenia		Bipolar Disease	
		Initial Dose	Maintenance Dose	Initial Dose	Maintenance Dose
First Generation Antipsychotics					
chlorpromazine	0.5 mg/kg 2 to 3 hours before operation (preoperative apprehension); 0.5 mg/kg every 4 to 6 hours as needed (N/V); 0.5 mg/kg every 4 to 6 hours (severe behavioral problems)	--	--	--	--
haloperidol	0.05 to 0.075 mg/kg/day (Tourette's disorder, non-psychotic behavior disorders/hyperactivity)	0.5 mg daily	0.15 mg/kg/day in divided doses	--	--
molindone	--	See adult dosing	See adult dosing	--	--
perphenazine	See adult dosing (N/V)	See adult dosing	See adult dosing	--	--
pimozide (Orap)	0.05 mg/kg/day up to 0.2 mg/kg/day (Tourette's disorder)*	--	--	--	--
thioridazine	--	0.5 mg/kg/day in divided doses	3 mg/kg/day in divided doses	--	--
thiothixene	--	See adult dosing	See adult dosing	--	--
trifluoperazine	--	1 mg once or twice daily†	Up to 15 mg daily†	--	--

Antipsychotics – Dosing & Availability (Pediatrics)

Drug	Other Indications	Schizophrenia		Bipolar Disease	
		Initial Dose	Maintenance Dose	Initial Dose	Maintenance Dose
Second Generation Antipsychotics					
aripiprazole (Abilify)	Age 6 to 17 years: 2 mg daily	Age 6 to 17 years: 5 mg to 10 mg daily Maximum dose = 15 mg daily	Age 13 to 17 years: 2 mg daily	Age 13 to 17 years: 10 mg daily Maximum dose = 30 mg daily	Age 10 to 17 years: 2 mg daily
asenapine (Saphris)	--	--	--	--	Age 10–17 years: 2.5 mg twice daily
lurasidone (Latuda)	--	Age 13 to 17 years: 40 mg once daily	Age 13 to 17 years: 40 mg to 80 mg daily	Age 10 to 17 years: 20 mg once daily	Age 10 to 17 years: 20 mg to 40 mg once daily (max 80 mg daily)
olanzapine (Zyprexa)	--	--	Age 13 to 17 years: 2.5 mg to 5 mg daily	Age 13 to 17 years: 10 mg daily	Age 13 to 17 years: 2.5 mg to 5 mg daily
olanzapine/fluoxetine (Symbyax)	--	--	--	--	Age 10 to 17 years: 3/25 mg daily
paliperidone (Invega)	--	--	Age 12 to 17 years: Weight < 51 kg: 3 mg daily Weight ≥ 51 kg: 3 mg daily	Age 12 to 17 years: Weight < 51 kg: 3 mg to 6 mg daily Maximum dose = 6 mg daily Weight ≥ 51 kg: 3 mg to 12 mg daily Maximum dose = 12 mg daily	--
quetiapine (Seroquel)	--	--	Age 13 to 17 years: 25 mg twice daily	Age 13 to 17 years: 400 mg to 800 mg per day	Age 10 to 17 years: 25 mg twice daily
quetiapine (Seroquel XR)	--	--	Age 13 to 17 years: 50 mg to 400 mg per day	Age 13 to 17 years: 400 mg to 800 mg per day	Age 10 to 17 years: 50 mg to 400 mg per day
risperidone (Risperdal)	Age 5 to 17 years: Weight < 20 kg: 0.25 mg daily Weight ≥ 20 kg: 0.5 mg daily	Age 5 to 17 years: Weight < 20 kg: 0.5 mg daily after at least 4 days Weight ≥ 20 kg: 1 mg daily after at least 4 days Maintain for at least 14 days; If insufficient response, increase at ≥ 2 week intervals by 0.25 mg per day for weight < 20 kg or 0.5 mg per day for weight ≥ 20 kg (range, 0.5 to 3 mg/day)	Age 13 to 17 years: 0.5 mg daily	Age 13 to 17 years: 3 mg daily (range, 1 to 6 mg/day)	Age 10 to 17 years: 0.5 mg daily

Antimigraine Agents, Triptans & Others

Magellan Medicaid Administration

Antimigraine, Triptans & Others – Dosing & Availability

Drug	Availability	Single Initial Dose	Minimum Time Before Repeat Dose (hr)	Maximum Dose in 24 Hours (mg)	Package Size
almotriptan	6.25 mg, 12.5 mg tablets	6.25 mg or 12.5 mg	2	25	1, 6 (6.25 mg only), 12 (12.5 mg only)
eletriptan (Relpax)	20 mg, 40 mg tablets	20 mg or 40 mg	2	80	1, 6, 12 (40 mg only)
frovatriptan (Frova)	2.5 mg tablet	2.5 mg	2	7.5	1, 9 (brand only)
naratriptan (Amerge)	1 mg, 2.5 mg tablets	1 mg or 2.5 mg	4	5	1, 9 (generic only)
rizatriptan (Maxalt, Maxalt-MLT)	5 mg, 10 mg tablets	5 mg or 10 mg (pediatrics weight based: 5 mg < 40 kg; 10 mg ≥ 40 kg)	2 (adults); Subsequent redosing not established in children	30 (adults), 5 to 10mg (children)	Tablets: 5 mg (generic only): 1, 12, 18, 30 10 mg: 1, 12, 18, 30 MLTs (orally disintegrating tablets [ODTs]): 5 mg: 1, 3, 9, 12, 18 10 mg: 1, 3, 9, 12, 18
sumatriptan (Imitrex)	4 mg, 6 mg injection	4 mg, 6 mg SC	1	12	Injection: 4 or 6 mg/0.5 mL Injection kit STATdose system (2 prefilled cartridges + 1 pen); STATdose cartridges (2 prefilled cartridges for refill) Vials: 6 mg injections only (5 single-dose vial cartons)
sumatriptan (Onzetra Xsail)	4 mg, 6 mg injection (needle-free system)	4 mg, 6 mg SC	1	12	Two 4 or 6 mg/0.5 mL single-dose pre-filled units
sumatriptan (Sumavel DosePro)	3 mg injection	3 mg SC	1 may be given ≥ 1 hour after a dose of another sumatriptan product	12	Four 3 mg/0.5 mL prefilled auto-injectors
sumatriptan (Zembrace SymTouch)	11 mg per single-use nosepiece	22 mg (2 nosepieces)	2	44	8 doses (16 nose-pieces) per kit

Antimigraine, Triptans & Others – Dosing & Availability

Drug	Availability	Single Initial Dose	Minimum Time Before Repeat Dose (hr)	Maximum Dose in 24 Hours (mg)	Package Size
sumatriptan nasal powder (Onzetra Xsail)	11 mg per single-use nosepiece	22 mg (2 nosepieces)	2	44	8 doses (16 nose-pieces) per kit
sumatriptan nasal spray (Imitrex)	5 mg, 20 mg per spray	5 mg or 10 mg (1 to 2 sprays) or 20 mg (1 spray)	2	40	1, 6
sumatriptan tablet (Imitrex)	25 mg, 50 mg, 100 mg tablets	25 mg to 100 mg	2	200	1, 9, 36, 90, 100
sumatriptan/ naproxen (Treximet)	10 mg/60 mg (brand only), 85 mg/500 mg tablets	Pediatric: 10/60 mg Adult: 85/500 mg	2	Pediatric: 1 tablet of 85/500 mg Adult: 2 tablets of 85/500 mg	9
sumatriptan; camphor/ menthol (Migranow Kit)	50 mg sumatriptan tablets; 4% camphor/10% menthol gel	Tablets: 25 mg to 100 mg; Gel: using liberal amount, apply directly on affected area (avoiding eyes or mucous membranes)	Tablets: 2; Gel: no time interval specified	Tablets: 200; Gel: 3 to 4 uses/day	1-kit: nine 50 mg sumatriptan tablets co-packaged with 3 oz (85 g) of Camphotrex Extra Strength gel (4% camphor/10% menthol) with roll-on applicator
zolmitriptan (Zomig, ZMT)	2.5 mg, 5 mg tablets and ODTs	2.5 mg or 5 mg	2	10	Tablets: 2.5 mg: 1, 6; 5 mg: 1, 3 ZMT (ODT): 2.5 mg: 1, 6; 5 mg: 1, 3
zolmitriptan nasal spray (Zomig)	2.5 mg, 5 mg per spray	2.5 mg	2	10	6-single dose nasal spray units in 2 mg or 5 mg strengths (brand only)

Magellan Rx MANAGEMENT℠

Magellan Medicaid Administration

Antihypertensives (Angiotensin Modulators, Beta Blockers, Calcium Channel Blockers, Diuretics)

Angiotensin Modulators – Dosing & Availability

Drugs	Initial Hypertension Dosage	Hypertension Dosage Range	Type 2 Diabetic Nephropathy Dosage Range	Risk Reduction	CHF	Post MI	Dose for Volume-or salt-depleted patients	Availability
Angiotensin II Receptor Blockers: Single Agents								
azilsartan (Edarbi)	80 mg once daily	40 mg to 80 mg once daily	--	--	--	--	no dosage recommendation	40 mg, 80 mg tablets
candesartan (Atacand)	16 mg once daily; Pediatrics: 1 to < 6 years: 0.2 mg/kg once daily; 6 to < 17 years: < 50 kg weight: 4 mg to 8 mg once daily; > 50 kg weight: 8 mg to 16 mg once daily*	8 mg to 32 mg; Pediatrics: 1 to < 6 years: 0.05 to 0.4 mg/kg daily; 6 to < 17 years: < 50 kg weight: 4 mg to 16 mg daily; > 50 kg weight: 4 mg to 32 mg daily May give doses divided once or twice daily	--	--	4 mg to 32 mg once daily	--	no dosage recommendation†	4 mg, 8 mg, 16 mg, 32 mg tablets
eprosartan	600 mg once daily	400 mg to 800 mg per day; divided doses once or twice daily	--	--	--	--	no dosage recommendation†	600 mg tablets
irbesartan (Avapro)	150 mg once daily	75 mg to 300 mg once daily	300 mg once daily	--	--	--	75 mg once daily	75 mg, 150 mg, 300 mg tablets
losartan (Cozaar)	50 mg once daily Pediatrics (6 to 16 years): 0.7 mg/kg/day (or 50 mg daily)	25 mg to 100 mg per day; divided doses once or twice daily Pediatrics (6 to 16 years): 0.7 mg/kg/day (or 50 mg daily) to max of 1.4 mg/kg/day or 100 mg daily	50 mg to 100 mg once daily	Reduction of stroke risk with HTN and LVH: 50 mg to 100 mg daily	--	--	25 mg once daily	25 mg, 50 mg, 100 mg tablets
olmesartan (Benicar)	20 mg once daily Pediatrics (6 to 16 years): < 35 kg 10 mg once daily; ≥ 35 kg 20 mg once daily*	20 mg to 40 mg once daily Pediatrics (6 to 16 years): < 35 kg 10 to 20 mg once daily; ≥ 35 kg 20 to 40 mg once daily*	--	--	--	--	no dosage recommendation†	5 mg, 20 mg, 40 mg tablets

Angiotensin Modulators – Dosing & Availability

Drugs	Initial Hypertension Dosage	Hypertension Dosage Range	Type 2 Diabetic Nephropathy Dosage Range	Risk Reduction	CHF	Post MI	Dose for Volume-or salt-depleted patients	Availability
Angiotensin II Receptor Blockers: Single Agents (*continued*)								
telmisartan (Micardis)	40 mg once daily	20 mg to 80 mg once daily	--	CV risk reduction: 80 mg once daily	--	--	no dosage recommendation	20 mg, 40 mg, 80 mg tablets
valsartan (Diovan)	80 mg to 160 mg once daily	80 mg to 320 mg once daily Pediatrics (6 to 16 years): 1.3 to 2.7 mg/kg once daily (40 mg to 160 mg)	--	--	40 mg to 160 mg twice daily	20 mg to 160 mg twice daily	no dosage recommendation	40 mg, 80 mg, 160 mg, 320 mg tablets
Angiotensin II Receptor Blockers: Combination Products								
azilsartan/ chlorthalidone (Edarbyclor)	40/12.5 mg once daily	40/12.5 mg to 40/25 mg once daily	--	--	--	--	--	40/12.5 mg, 40/25 mg tablets
candesartan/HCTZ (Atacand HCT)	16/12.5 mg once daily	16/12.5 mg to 32/25 mg per day	--	--	--	--	--	16/12.5 mg, 32/12.5 mg, 32/25 mg tablets
irbesartan/ HCTZ (Avalide)	150/12.5 mg once daily	150/12.5 mg to 300/25 mg once daily	--	--	--	--	--	150/12.5 mg, 300/12.5 mg tablets
losartan/HCTZ (Hyzaar)	50/12.5 mg once daily	50/12.5 mg once or twice daily or 100/25 mg once daily	--	--	--	--	--	50/12.5 mg, 100/12.5 mg, 100/25 mg tablets
olmesartan/ HCTZ (Benicar HCT)	20/12.5 mg once daily	20/12.5 mg to 40/25 mg once daily	--	--	--	--	--	20/12.5 mg, 40/12.5 mg, 40/25 mg tablets

Angiotensin Modulators – Dosing & Availability

Drugs	Initial Hypertension Dosage	Hypertension Dosage Range	Type 2 Diabetic Nephropathy Dosage Range	Risk Reduction	CHF	Post MI	Dose for Volume- or salt-depleted patients	Availability
Angiotensin II Receptor Blockers: Combination Products								
sacubitril/valsartan (Entresto)	--	--	--	--	Adults - Initial: 49/51 mg twice daily Range: 24/26 mg to 97/103 mg twice daily Pediatrics (ages ≥ 1 year) •Body weight < 40 kg: initial: 1.6 mg/kg twice daily; Range: 2.3 to 3.1 mg/kg twice daily •Body weight 40 kg to < 50 kg: initial: 24/26 mg twice daily; Range: 49/51 mg to 72/78 mg •Body weight ≥ 50 kg: initial 49/51 mg; Range: 72/78 mg to 97/103 mg	--	--	24/26 mg, 49/51 mg, 97/103 mg tablets
telmisartan/ HCTZ (Micardis HCT)	40/12.5 mg once daily	40/12.5 mg to 160/25 mg once daily	--	--	--	--	--	40/12.5 mg, 80/12.5 mg, 80/25 mg tablets
valsartan/HCTZ (Diovan HCT)	160/12.5 mg once daily	80/12.5 mg to 320/25 mg once daily	--	--	--	--	--	80/12.5 mg, 160/12.5 mg, 160/25 mg, 320/12.5 mg, 320/25 mg tablets

Angiotensin Modulators - Dosing & Availability

Drugs	Dosage	Combinations Available (Calcium Channel Blocker/Angiotensin Modulator)
amlodipine/benazepril (Lotrel)	**X**	2.5/10 mg (generic only), 5/10 mg, 5/20 mg, 10/20 mg, 5/40 mg (generic only), 10/40 mg capsules
amlodipine/olmesartan (Azor)	**X**	5/20 mg, 5/40 mg, 10/20 mg, 10/40 mg tablets
amlodipine/olmesartan/HCTZ (Tribenzor)	**X**	5/20/12.5 mg, 5/40/12.5 mg, 5/40/25 mg, 10/40/12.5 mg, 10/40/25 mg tablets
amlodipine/perindopril (Prestalia)	**---**	2.5/3 mg, 5/7 mg, 10/14 mg tablets
amlodipine/telmisartan (Twynsta)	**X**	5/40 mg, 5/80 mg, 10/40 mg, 10/80 mg
amlodipine/valsartan (Exforge)	**X**	5/160 mg, 5/320 mg, 10/160 mg, 10/320 mg tablets
amlodipine/valsartan/HCTZ (Exforge HCT)	**X**	5/160/12.5 mg, 5/160/25 mg, 10/160/12.5 mg, 10/160/25 mg, 10/320/25 mg tablets
nebivolol/valsartan (Byvalson)	**---**	5/80 mg tablets
verapamil sustained-release (SR) /trandolapril (Tarka)	**X**	180/2 mg, 240/1 mg, 240/2 mg, 240/4 mg tablets

Beta Blockers - Dosing & Availability

Drugs	HTN	Angina Pectoris	Heart Failure	Other Indications	Availability
acebutolol (Sectral)	200–400 mg twice daily	-	-	See package insert for other indications	200 mg, 400 mg capsule
atenolol (Tenormin)	50–100 mg daily	50–200 mg daily	-	MI: 50 mg twice daily or 100 mg daily	25 mg, 50 mg, 100 mg tablets
betaxolol	10–20 mg daily	-	-	-	10 mg, 20 mg tablets
bisoprolol	2.5–20 mg daily	-	-	-	5 mg, 10 mg tablets
carvedilol (Coreg)	6.25–25 mg twice daily	-	3.125–25 mg twice daily	LVD following MI: 3.125–25 mg twice daily	3.125 mg, 6.25 mg, 12.5 mg, 25 mg tablets
carvedilol CR (Coreg CR)	20–80 mg once daily	-	10–80 mg once daily	LVD following MI: 20–80 mg once daily	10 mg, 20 mg, 40 mg, 80 mg capsules
labetalol	100–400 mg twice daily	-	-	-	100 mg, 200 mg, 300 mg tablets
metoprolol succinate ER (Toprol XR, Kapspargo Sprinkle)	25–400 mg daily	100–400 mg daily	*12.5 - 200 mg daily	-	25 mg, 50 mg, 100 mg, 200 mg tablets and sprinkle capsules
metoprolol tartrate (Lopressor)	100–450 mg daily	50 mg twice daily to 400 mg daily	-	MI: 25–50 mg every 6 hours, then 100 mg twice daily	25 mg, 37.5 mg, 50 mg, 75 mg, 100 mg tablets
nadolol (Corgard)	40–320 mg daily	40–240 mg daily	-	-	20 mg, 40 mg, 80 mg tablets
nebivolol (Bystolic)	5–40 mg daily	-	-	-	2.5 mg, 5 mg, 10 mg, 20 mg tablets

Beta Blockers - Dosing & Availability

Drugs	HTN	Angina Pectoris	Heart Failure	Other Indications	Availability
pindolol	5 mg twice daily to 60 mg daily	-	-	-	5 mg, 10 mg tablets
propranolol	40 mg twice daily initially, then 120–240 mg/day in divided doses	80–320 mg daily in divided doses	-	See package insert for other indications	10 mg, 20 mg, 40, 60 mg, 80 mg tablets; 20 mg/5 mL, 40 mg/5 mL oral solution
propranolol (Hemangeol)	-	-	-	Infantile hemangioma: initiate at ages 5 weeks to 5 months at 0.15 mL/kg (0.6 mg/kg) twice daily; adjust to maintenance dose of 0.4 mL/kg (1.7 mg/kg) twice daily; administer at least 9 hours apart during or after feeding; monitor heart rate and blood pressure for 2 hours after the first dose or increasing dose	4.28 mg/mL oral solution (120 mL bottle)
propranolol ER (Innopran XL)	80 or 120 mg at bedtime	-	-	-	80 mg, 120 mg capsules
propranolol ER (Inderal XL)	80 or 120 mg at bedtime	-	-	-	80 mg, 120 mg capsules
propranolol LA (Inderal LA)	80 mg daily, then 120–160 mg daily	80–320 mg daily	-	See package insert for other indications	60 mg, 80 mg, 120 mg, 160 mg capsules
sotalol (Betapace)	-	-	-	See package insert for other indications	80 mg, 120 mg, 160 mg, 240 mg tablets
sotalol AF (Betapace AF)	-	-	-	See package insert for other indications	80 mg, 120 mg, 160 mg tablets
sotalol (Sotylize)	-	-	-	See package insert for other indications	5 mg/mL oral solution
timolol	10–30 mg twice daily	-	-	MI: 10 mg twice daily See package insert for other indications	5 mg, 10 mg, 20 mg tablets

Beta Blockers - Dosing & Availability

Drugs	Initial HTN Dosage	Maximum HTN Dosage	Availability
atenolol / chlorthalidone (Tenoretic)	50/25 mg once daily	100/25 mg once daily	50/25 mg, 100/25 mg tablets
bisoprolol / hydrochlorothiazide (Ziac)	2.5/6.25 mg once daily	20/12.5 mg once daily	2.5/6.25 mg, 5/6.25 mg, 10/6.25 mg tablets
metoprolol succinate / hydrochlorothiazide (Dutoprol)	Individualized based on baseline and target blood pressure, as well as previous experience with antihypertensives	200/25 mg once daily (two 100/12.5 mg tablets)	25/12.5 mg, 50/12.5 mg, 100/12.5 mg tablets
metoprolol tartrate / hydrochlorothiazide	50/25 mg twice daily	100/25 mg given as 1–2 tablets in a single or divided doses 100/50 mg given a single dose	50/25 mg, 100/25 mg, 100/50 mg tablets
nadolol / bendroflumethiazide (Corzide)	40/5 mg once daily	80/5 mg once daily	40/5 mg, 80/5 mg tablets
propranolol / hydrochlorothiazide	40/25 mg twice daily	80/25 mg once or twice daily	40/25 mg, 80/25 mg tablets

Calcium Channel Blockers – Dosing & Availability

Drugs	Initial HTN Dose	Maximum HTN Dose	Angina Dose	Availability
Dihydropyridines				
amlodipine (Norvasc, Katerzia)	5 mg daily	10 mg daily	5-10 mg daily	2.5, 5, 10 mg tablets 1 mg/mL oral suspension
felodipine ER (Plendil)	5 mg daily	10 mg daily	--	2.5, 5, 10 mg tablets
isradipine	2.5 mg twice daily	10 mg twice daily	--	2.5, 5 mg capsules
nicardipine (Cardene)	20 mg three times a day	40 mg three times a day	20-40 mg three times a day	20, 30 mg capsules
nicardipine SR (Cardene SR)	30 mg twice daily	60 mg twice daily	--	30, 45, 60 mg capsules
nifedipine	--	--	10 mg three times a day to max of 30 mg per dose or 180 mg per day	10, 20 mg capsules
nifedipine SR	Adalat CC, Procardia XL: 30-60 mg daily	Adalat CC: 90 mg Procardia XL: 120 mg daily	Adalat CC, Procardia XL: 30-90 mg daily	ER tablet: 30, 60, 90 mg tablets Adalat CC, Procardia XL, Nifediac CC: 30, 60, 90 mg tablets Afeditab CR, Nifedical XL: 30, 60 mg tablets
nimodipine	--	--	--	30 mg capsules
nimodipine (Nymalize)	--	--	--	16 oz (473 mL) bottle 20 mL unit dose cup with 1 oral syringe
nisoldipine ER	20 mg daily	60 mg daily	--	ER tablet: 20, 30, 40 mg tablets
nisoldipine ER (Sular)	17 mg daily	34 mg daily	--	8.5, 17, 25.5, 34 mg tablets

Calcium Channel Blockers – Dosing & Availability

Drugs	Initial HTN Dose	Maximum HTN Dose	Angina Dose	Availability
Non-dihydropyridines				
diltiazem (Cardizem)	--	--	30 mg four times daily to a max of 360 mg per day	30, 60, 90, 120 mg tablets
diltiazem ER	120-240 mg daily	480 mg daily Tiazac: 540 mg daily	120-480 mg daily Tiazac: 120-540 mg daily	ER capsules: 120, 180, 240, 300, 360, 420 mg capsules Cardizem CD, Cartia XT, Dilacor XR, Diltia XT, Dilt CD, Dilt XR, Taztia XT, Tiazac: 120, 180, 240 mg capsules Cardizem CD, Cartia XT, Dilt CD, Taztia XT, Tiazac: 300 mg capsules Cardizem CD, Taztia XT, Tiazac: 360 mg capsules Tiazac: 420 mg capsules
diltiazem ER (Cardizem LA, Matzim LA)	180-240 mg daily	540 mg daily	180-360 mg daily	120, 180, 240, 300, 360, 420 mg tablets
verapamil (Calan)	80 mg three times daily	480 mg per day	80 mg-120 mg three times daily up to a max of 480 mg per day	40, 80, 120 mg tablets
verapamil ER (Covera HS)	180 mg at bedtime	480 mg at bedtime	180-480 mg at bedtime	180, 240 mg tablets
verapamil ER (Verelan PM)	200 mg at bedtime	400 mg at bedtime	--	100, 200, 300 mg capsules
verapamil SR	240 mg daily	480 mg daily	--	Calan SR, Isoptin SR: 120, 180, 240 mg tablets
verapamil SR (Verelan)	240 mg daily	480 mg daily	--	120, 180, 240, 360 mg capsules

Diuretics – Current Product Listing

Diuretics, Appendix A; Current Product Listing

LABEL NAME	MANUFACTURER	DRUG TYPE	PROVIDER SYNERGIES BNRT
ALDACTAZIDE 25-25 TABLET	PHARMACIA/UPJHN	BWG	ALDACTAZIDE (ORAL)
ALDACTAZIDE 50-50 TABLET	PHARMACIA/UPJHN	BWG	ALDACTAZIDE (ORAL)
ALDACTONE 100 MG TABLET	PHARMACIA/UPJHN	BWG	ALDACTONE (ORAL)
ALDACTONE 25 MG TABLET	PHARMACIA/UPJHN	BWG	ALDACTONE (ORAL)
ALDACTONE 50 MG TABLET	PHARMACIA/UPJHN	BWG	ALDACTONE (ORAL)
AMILORIDE HCL 5 MG TABLET	PADDOCK LABS.	GEN	AMILORIDE (ORAL)
AMILORIDE HCL-HCTZ 5-50 MG TAB	MYLAN	GEN	AMILORIDE HCTZ (ORAL)
BUMETANIDE 0.5 MG TABLET	NORTHSTAR RX LL	GEN	BUMETANIDE (ORAL)
BUMETANIDE 1 MG TABLET	NORTHSTAR RX LL	GEN	BUMETANIDE (ORAL)
BUMETANIDE 2 MG TABLET	NORTHSTAR RX LL	GEN	BUMETANIDE (ORAL)
CAROSPIR 25 MG/5 ML SUSPENSION	CMP PHARMA, INC	SSB	CAROSPIR (ORAL)
CHLOROTHIAZIDE 250 MG TABLET	MYLAN	GEN	CHLOROTHIAZIDE (ORAL)
CHLOROTHIAZIDE 500 MG TABLET	MYLAN	GEN	CHLOROTHIAZIDE (ORAL)
CHLORTHALIDONE 25 MG TABLET	DR.REDDY'S LAB	GEN	CHLORTHALIDONE (ORAL)
CHLORTHALIDONE 50 MG TABLET	DR.REDDY'S LAB	GEN	CHLORTHALIDONE (ORAL)
DEMADEX 10 MG TABLET	MEDA PHARMACEUT	BWG	DEMADEX (ORAL)
DIURIL 250 MG/5 ML ORAL SUSP	SALIX PHARMACEU	SSB	DIURIL (ORAL)
DYAZIDE 37.5-25 CAPSULE	GLAXOSMITHKLINE	BWG	DYAZIDE (ORAL)
EDECRIN 25 MG TABLET	VALEANT	BWG	EDECRIN (ORAL)
EPLERENONE 25 MG TABLET	ACCORD HEALTHCA	GEN	EPLERENONE (ORAL)
EPLERENONE 50 MG TABLET	ACCORD HEALTHCA	GEN	EPLERENONE (ORAL)
ETHACRYNIC ACID 25 MG TABLET	AMNEAL PHARMACE	GEN	ETHACRYNIC ACID (ORAL)
FUROSEMIDE 10 MG/ML SOLUTION	MORTON GROVE PH	GEN	FUROSEMIDE SOLUTION (ORAL)
FUROSEMIDE 20 MG TABLET	SOLCO HEALTHCAR	GEN	FUROSEMIDE TABLET (ORAL)
FUROSEMIDE 40 MG TABLET	SOLCO HEALTHCAR	GEN	FUROSEMIDE TABLET (ORAL)
FUROSEMIDE 40 MG/5 ML SOLN	ROXANE LABS.	GEN	FUROSEMIDE SOLUTION (ORAL)
FUROSEMIDE 80 MG TABLET	SOLCO HEALTHCAR	GEN	FUROSEMIDE TABLET (ORAL)
HYDROCHLOROTHIAZIDE 12.5 MG CP	SCIEGEN PHARMAC	GEN	HYDROCHLOROTHIAZIDE CAPSULE (ORAL)
HYDROCHLOROTHIAZIDE 25 MG TAB	SOLCO HEALTHCAR	GEN	HYDROCHLOROTHIAZIDE TABLET (ORAL)
HYDROCHLOROTHIAZIDE 50 MG TAB	SOLCO HEALTHCAR	GEN	HYDROCHLOROTHIAZIDE TABLET (ORAL)

Diuretics – Current Product Listing

INDAPAMIDE 1.25 MG TABLET	ANI PHARMACEUTI	GEN	INDAPAMIDE (ORAL)
INDAPAMIDE 2.5 MG TABLET	ANI PHARMACEUTI	GEN	INDAPAMIDE (ORAL)
INSPRA 25 MG TABLET	PFIZER US PHARM	BWG	INSPRA (ORAL)
INSPRA 50 MG TABLET	PFIZER US PHARM	BWG	INSPRA (ORAL)
LASIX 20 MG TABLET	VALIDUS PHARMAC	BWG	LASIX (ORAL)
LASIX 40 MG TABLET	VALIDUS PHARMAC	BWG	LASIX (ORAL)
LASIX 80 MG TABLET	VALIDUS PHARMAC	BWG	LASIX (ORAL)
MAXZIDE 37.5 MG-25 MG TABLET	MYLAN	BWG	MAXZIDE-25 MG (ORAL)
MAXZIDE 75 MG-50 MG TABLET	MYLAN	BWG	MAXZIDE (ORAL)
METHYCLOTHIAZIDE 5 MG TABLET	MYLAN	SSB	METHYCLOTHIAZIDE (ORAL)
METOLAZONE 10 MG TABLET	LANNETT CO. INC	GEN	METOLAZONE (ORAL)
METOLAZONE 2.5 MG TABLET	LANNETT CO. INC	GEN	METOLAZONE (ORAL)
METOLAZONE 5 MG TABLET	LANNETT CO. INC	GEN	METOLAZONE (ORAL)
MICROZIDE 12.5 MG CAPSULE	ACTAVIS U.S. BR	BWG	MICROZIDE (ORAL)
SPIRONOLACTONE 100 MG TABLET	ZYDUS PHARMACEU	GEN	SPIRONOLACTONE (ORAL)
SPIRONOLACTONE 25 MG TABLET	ZYDUS PHARMACEU	GEN	SPIRONOLACTONE (ORAL)
SPIRONOLACTONE 50 MG TABLET	ZYDUS PHARMACEU	GEN	SPIRONOLACTONE (ORAL)
SPIRONOLACTONE-HCTZ 25-25 TAB	MYLAN INSTITUTI	GEN	SPIRONOLACTONE HCTZ (ORAL)
TORSEMIDE 10 MG TABLET	CITRON PHARMA L	GEN	TORSEMIDE (ORAL)
TORSEMIDE 100 MG TABLET	CITRON PHARMA L	GEN	TORSEMIDE (ORAL)
TORSEMIDE 20 MG TABLET	CITRON PHARMA L	GEN	TORSEMIDE (ORAL)
TORSEMIDE 5 MG TABLET	CITRON PHARMA L	GEN	TORSEMIDE (ORAL)
TRIAMTERENE-HCTZ 37.5-25 MG CP	LANNETT CO. INC	GEN	TRIAMTERENE-HCTZ (ORAL)
TRIAMTERENE-HCTZ 50-25 MG CAP	SANDOZ	GEN	TRIAMTERENE-HCTZ (ORAL)
TRIAMTERENE-HCTZ 75-50 MG TAB	BLUEPOINT LABOR	GEN	TRIAMTERENE-HCTZ (ORAL)

Pulmonary Hypertension

Magellan Medicaid Administration

Pulmonary Arterial Hypertension – Dosing & Availability

Drug	Initial Dose	Maximum Daily Dose	Availability
		Oral Agents	
ambrisentan (Letairis)	5 mg once daily with or without food	10 mg once daily	5 mg, 10 mg tablets
bosentan (Tracleer)	≤ 12 years of age: ≥ 4 - 8 kg; 16 mg twice daily, > 8 – 16 kg; 32 mg twice daily, > 16 – 24 kg; 48 mg twice daily, > 24 – 40 kg; 64 mg twice daily ≥ 12 years of age: 62.5 mg twice daily for first 4 weeks	≤ 12 years of age: 64 mg twice daily ≥ 12 years of age: 125 mg twice daily	32 mg tablet for oral suspension 62.5 mg, 125 mg tablets
macitentan (Opsumit)	10 mg once daily with or without food	10mg once daily	10 mg tablets
riociguat (Adempas)	1 mg three times a day with or without food	2.5 mg three times a day	0.5 mg, 1 mg, 1.5 mg, 2 mg, 2.5 mg tablets
selexipag (Uptravi)	200 mcg twice daily with or without food	– 1,600 mcg twice daily	Titration Pack: 200 mg, 800 mcg tablets 200 mg, 400 mg, 600 mg, 800 mg, 1,000 mg, 1,200 mg, 1,400 mg, 1,600 mcg tablets
sildenafil (Revatio)	Oral: 5 mg or 20 mg three times, 4 to 6 hours apart daily Injectable: 2.5 mg or 10 mg three times daily as intravenous bolus	Oral: 20 mg three times daily	20 mg tablet 10mg/mL oral suspension 10 mg (12.5 mL) single-use vial
tadalafil (Adcirca)	40 mg once daily with or without food	40 mg once daily with or without food	20 mg tablet
treprostinil (Orenitram)	0.25 mg twice daily with food	Determined by tolerability	0.125 mg, 0.25 mg, 1 mg, 2.5 mg, 5 mg extended-release tablets
		Inhalation Agents	
iloprost (Ventavis)	2.5 mcg/dose; if tolerated increase to 5 mcg/dose. Administer 6 to 9 times daily (dosing intervals 2 hours while awake according to individual need and tolerability)	45 mcg (or 5 mcg nine times daily)	10 mcg/mL (30 single use 1 ml ampules) and 20 mcg/mL (30 single use 1 mL ampules) oral inhalation solution
treprostinil (Tyvaso)	18 mcg (3 inhalations) four times daily about 4 hours apart; if 3 inhalations not tolerated reduce to 1 to 2 inhalations as tolerated	54 mcg (or 9 inhalations) four times daily	2.9 mL ampule containing 1.74 mg of treprostinil (0.6 mg per mL) oral inhalation solution Starter Kit contains 28 ampules and the Tyvaso Inhalation System Refill Kit contains 28 ampules and administration accessories

Pulmonary Arterial Hypertension – Indications

Drug	Dosage	Availability
Prostanoids		
epoprostenol (Flolan)	• Initiate chronic infusion of Flolan through a central venous catheter at 2 ng/kg/min and increase in increments of 2 ng/kg/min every 15 minutes or longer until dose-limiting pharmacologic effects are elicited or until a tolerance limit to the drug is established or further increases in the infusion rate are not clinically warranted	Powder for injection: • 0.5 mg/vial • 1.5 mg/vial • 50 mL of sterile diluent
epoprostenol (Veletri)	• Continuous infusion of Veletri should be initiated via a central venous catheter at 2 ng/kg/min and increase in increments of 2 ng/kg/min every 15 minutes or longer until dose-limiting pharmacologic effects are elicited or until a tolerance limit to the drug is established; If symptoms of pulmonary hypertension persist or recur after improving, the infusion should be increased by 1 to 2 ng/kg/min increments at 15 minute intervals	Powder for injection: • 0.5 mg/vial • 1.5 mg/vial
treprostinil (Remodulin)	• Treprostinil should be administered subcutaneously (SC) or intravenously (if SC is not tolerated) via continuous infusion. Infuse at 1.25ng/kg/min. If this initial dose cannot be tolerated because of systemic effects, the infusion rate should be reduced to 0.625ng/kg/min • For patients transitioning to an implantable intravenous (IV) infusion pump, the initial dose should be the same as the current dose • IV infusion rate should be increased in increments of 1.25ng/kg/min per week for the first four weeks of treatment and then 2.5ng/kg/min per week for the remaining duration of infusion	Solution for injection: 20 mL multi-dose vial in concentrations of • 1 mg/mL • 2.5 mg/mL • 5 mg/mL • 10 mg/mL
Phosphodiesterase type 5 (PDE-5) inhibitor		
sildenafil (Revatio)	Oral dosage: • 5 mg or 20 mg 3 times a day, 4 to 6 hours apart Injection: • For patients who are temporarily unable to take oral medication. • 2.5 mg or 10 mg administered as an IV bolus injection 3 times a day	Tablet: • 20 mg Oral suspension: • 10 mg/mL Solution for injection: • 10 mg/12.5 mL

Magellan Rx MANAGEMENT℠

Magellan Medicaid Administration

Bone Density Regulators (Bone Resorption Suppression and Related Agents)

Bone Resorption Inhibitors – Dosing & Availability

Drug	Treatment of osteoporosis in postmenopausal women	Prevention of osteoporosis in postmenopausal women	Treatment to increase bone mass in men with osteoporosis	Treatment of glucocorticoid-induced osteoporosis	Paget's disease	Availability
Bisphosphonates						
alendronate (Binosto)	70 mg once per week	--	70 mg once per week	--	--	70 mg effervescent tablets
alendronate (Fosamax)	10 mg per day or 70 mg once per week	5 mg per day or 35 mg once per week	10 mg per day or 70 mg once per week	5 mg per day, For post-menopausal women not receiving estrogen: 10 mg once daily	40 mg per day for 6 months May retreat if relapse occurs following a 6-month post-treatment evaluation	70 mg tablets 5 mg, 10 mg, 35 mg, 40 mg, tablets (generics only) 70 mg/75 mL oral solution (generic only)
alendronate /vitamin D (Fosamax Plus D)	70 mg/2,800 IU or 70 mg/5,600 IU weekly	--	70 mg/2,800 IU or 70 mg/5,600 IU weekly	--	--	70 mg/ 2,800 IU, 70 mg/ 5,600 IU tablets
etidronate	--	--	--	--	5-10 mg/kg/day up to 6 months or 11-20 mg/kg/day up to 3 months May retreat if relapse occurs following a 90 day post-treatment evaluation	200 mg, 400 mg tablets
ibandronate (Boniva)	2.5 mg per day or 150 mg per month	2.5 mg per day or 150 mg per month	--	--	--	2.5 mg tablets (brand only), 150 mg tablets
risedronate (Actonel)	5 mg per day or 35 mg once per week or 75 mg for 2 consecutive days every month or 150 mg once a month	5 mg per day or 35 mg once per week or 75 mg for 2 consecutive days every month or 150 mg once a month	35 mg once per week	5 mg per day	30 mg per day for 2 months May retreat if relapse occurs, after a 2-month post-treatment observation.	5 mg, 30 mg, 35 mg, and 150 mg tablets
risedronate delayed-release (Atelvia)	35 mg once weekly	--	--	--	--	35 mg delayed-release tablets

Bone Resorption Inhibitors – Dosing & Availability

Drug	Treatment of osteoporosis in postmenopausal women	Prevention of osteoporosis in postmenopausal women	Treatment to increase bone mass in men with osteoporosis	Treatment of glucocorticoid-induced osteoporosis	Paget's disease	Availability
Calcitonins						
calcitonin-salmon	200 IU intranasally per day, alternating nostrils daily	--	--	--	--	3.7 mL (30 dose) bottle
Others						
abaloparatide (Tymlos)	80 mcg SC per day	--	--	--	--	3,120 mcg/1.56 mL prefilled pen
denosumab (Prolia)	60 mg SC every 6 months, administered by a healthcare professional	--	60 mg SC every 6 months; administered by a healthcare professional	60 mg SC every 6 months; administered by a healthcare professional	--	60 mg/1 mL single use pre-filled syringe
raloxifene (Evista)	60 mg per day	60 mg per day	--	--	--	60 mg tablets
teriparatide (Forteo)	20 mcg SC per day	--	20 mcg SC per day	20 mcg SC per day	--	600 mcg/2.4 mL prefilled pen
romosozumab-aqqg (Evenity)	210 mg (as 2 consecutive 105 mg injections) SC per month, administered by a healthcare professional; duration is 12 monthly doses	--	--	--	--	105 mg/1.17 ml pre-filled syringe

Bone Resorption Inhibitors, IV – Dosing & Availability

Bone Resoprtion Inhibitors, IV; Current Product Listing

LABEL NAME	MANUFACTURER	DRUG TYPE	PROVIDER SYNERGIES BRAND NAME ROUTE
IBANDRONATE 3 MG/3 ML SYRINGE	generic	GEN	IBANDRONATE (INTRAVEN)
IBANDRONATE 3 MG/3 ML VIAL	SUN PHARMACEUTI	GEN	IBANDRONATE (INTRAVEN)
MIACALCIN 400 UNIT/2 ML VIAL	MYLAN INSTITUTI	SSB	MIACALCIN (INJECTION)
PAMIDRONATE 30 MG/10 ML VIAL	generic	GEN	PAMIDRONATE DISODIUM (INTRAVEN)
PAMIDRONATE 60 MG/10 ML VIAL	HOSPIRA/PFIZER	GEN	PAMIDRONATE DISODIUM (INTRAVEN)
PAMIDRONATE 90 MG/10 ML VIAL	generic	GEN	PAMIDRONATE DISODIUM (INTRAVEN)
PAMIDRONATE DISOD 30 MG VIAL	AREVA PHARMACEU	GEN	PAMIDRONATE DISODIUM (INTRAVEN)
PAMIDRONATE DISOD 90 MG VIAL	AREVA PHARMACEU	GEN	PAMIDRONATE DISODIUM (INTRAVEN)
XGEVA 120 MG/1.7 ML VIAL	AMGEN	SSB	XGEVA (SUB-Q)
ZOLEDRONIC ACID 5 MG/100 ML	generic	GEN	ZOLEDRONIC ACID (RECLAST) (INTRAVEN)
ZOLEDRONIC ACID 4 MG VIAL	SUN PHARMA GLOB	GEN	ZOLEDRONIC ACID (ZOMETA) (INTRAVEN)
ZOLEDRONIC ACID 4 MG/100 ML	generic	GEN	ZOLEDRONIC ACID (ZOMETA) (INTRAVEN)
ZOLEDRONIC ACID 4 MG/5 ML VIAL	generic	GEN	ZOLEDRONIC ACID (ZOMETA) (INTRAVEN)

Magellan Rx MANAGEMENT℠

Magellan Medicaid Administration

Antiemetics/Antivertigo Agents

Antiemetics Agents – Dosing & Availability

Drugs	Prevention of chemotherapy-induced N/V		Prevention of radiotherapy-induced N/V in adults or Other Use	Prevention of post-operative N/V		Availability
	Adult	Pediatric		Adult	Pediatric	
NK_1 receptor antagonists						
aprepitant (Emend)	125 mg 1 hour prior to chemotherapy day 1, then 80 mg once daily in the morning on days 2 and 3 as part of regimen including corticosteroid and a 5-HT3 antagonist (suspension may be used for those unable to use capsules)	Capsules (≥ 12 years old): dosing is the same as for adults Suspension (patients ≥ 6 months and ≥ 6 kg): 3 mg/kg (maximum 125 mg) 1 hour prior to chemotherapy day 1, then 2 mg/kg (maximum 80 mg) once daily in the morning on days 2 and 3 as part of regimen including corticosteroid and a 5-HT3 antagonist	--	40 mg within 3 hours prior to induction of anesthesia	--	capsules: 40 mg, 80 mg, 125 mg bi-fold pack: two 80 mg capsules tri-fold/tripack pack: one 125 mg capsule and two 80 mg capsules oral suspension: 125 mg packaged with oral dosing dispensers and a mixing cup (brand Emend only)

Antiemetics Agents – Dosing & Availability

Drugs	Prevention of chemotherapy-induced N/V		Prevention of radiotherapy-induced N/V in adults or Other Use	Prevention of post-operative N/V		Availability
	Adult	Pediatric		Adult	Pediatric	
NK_1 receptor antagonists						
aprepitant (Cinvanti)	Single dose regimen for highly emetogenic chemotherapy (HEC): 130 mg on day 1 of a 4 day regimen by injection over 2 minutes or as an IV infusion over 30 minutes, completing administration approximately 30 minutes prior to chemotherapy in combination with a corticosteroid and a 5-HT3 antagonist Regimen for moderately emetogenic chemotherapy (MEC): 100 mg on day 1 of a 3 day regimen by injection over 2 minutes or as an IV infusion over 30 minutes, completing administration approximately 30 minutes prior to chemotherapy in combination with a corticosteroid and a 5-HT3 antagonist (with oral aprepitant used on days 2 and 3)	--	--	--	--	Injectable emulsion: 130 mg/18 mL in a single-dose vial

Antiemetics Agents – Dosing & Availability

Drugs	Prevention of chemotherapy-induced N/V		Prevention of radiotherapy-induced N/V in adults or Other Use	Prevention of post-operative N/V		Availability
	Adult	Pediatric		Adult	Pediatric	
NK_1 receptor antagonists						
fosaprepitant (Emend for injection)	Single-dose regimen for highly emetogenic chemotherapy (HEC): 150 mg on day 1 of a 4 day regimen as an infusion over 20 to 30 minutes approximately 30 minutes prior to chemotherapy in combination with a corticosteroid (days 1-4) and a 5-HT3 antagonist (day 1) Single-dose regimen for moderately emetogenic chemotherapy (MEC): 150 mg on day 1 as an infusion over 20 to 30 minutes approximately 30 minutes prior to chemotherapy in combination with a corticosteroid and a 5-HT3 antagonist	Single-dose chemotherapy regimen: Age 12 to 17 years – infuse 115 mg over 30 minutes Age 6 months to <12 years – infuse 3 mg/kg (maximum 115 mg)over 60 minutes 3- day regimen: injection on day 1 (as dosed by age for single-dose regimens above) and the oral formulation on days 2 and 3 as	--	--	--	injection: 150 mg per single-use vial
rolapitant (Varubi)	Administer prior to the initiation of each cycle of chemotherapy without regard to food, but at no less than 2 week intervals; Rolapitant is to be used in combination with a 5-HT3 receptor antagonist and dexamethasone HEC: 180 mg (2 tablets) orally or 166.5 mg IV over 30 minutes administered 2 hours prior to chemotherapy on day 1 with a corticosteroid and a 5-HT3 antagonist (corticosteroid also administered days 2-4) MEC: 180 mg (2 tablets) orally or 166.5 mg IV over 30 minutes administered 2 hours prior to chemotherapy on day 1 with a corticosteroid and a 5-HT3 antagonist (5-HT3 antagonist administered per prescribing information)	--	--	--	--	tablets: 90 mg

Antiemetics Agents – Dosing & Availability

Drugs	Prevention of chemotherapy-induced N/V		Prevention of radiotherapy-induced N/V in adults or Other Use	Prevention of post-operative N/V		Availability
	Adult	Pediatric		Adult	Pediatric	
5-HT3 antagonists						
dolasetron (Anzemet)	100 mg orally within 1 hour before chemotherapy	2 to 16 years: 1.8 mg/kg (up to 100 mg) orally within 1 hour before chemotherapy	--	100 mg orally within 2 hours before surgery	2 to 16 years: 1.2 mg/kg orally (up to 100 mg) given within 2 hours before surgery	tablets: 50 mg, 100 mg
granisetron	Oral: 2 mg up to 1 hour before chemotherapy for 1 dose OR 1 mg up to 1 hour before chemotherapy followed by 1 mg 12 hours after the first dose Injectable: 10 mcg/kg IV given up to 30 minutes before initiation of chemotherapy only on the day(s) chemotherapy is given	Injectable (2 to 16 years): 10 mcg/kg	2 mg once daily taken within 1 hour of radiation	Injectable: Prevention: 1 mg IV over 30 seconds before induction or immediately before reversal of anesthesia. Treatment: 1 mg IV over 30 seconds	--	tablets: 1 mg injection: 0.1 mg/1 mL, 1 mg/1 mL, 4 mg/4 mL
granisetron transdermal (Sancuso)	Apply single patch to upper outer arm 24 hours prior to chemotherapy; remove 24 hours after completion of chemotherapy The patch can be worn for up to 7 days	--	--	--	--	transdermal patch containing 34.3 mg granisetron that releases 3.1 mg over 24 hours for 7 days

Antiemetics Agents – Dosing & Availability

Drugs	Prevention of chemotherapy-induced N/V		Prevention of radiotherapy-induced N/V in adults or Other Use	Prevention of post-operative N/V		Availability
	Adult	Pediatric		Adult	Pediatric	
5-HT3 antagonists						
granisetron injection, extended-release (Sustol)	10 mg as a single subcutaneous (SC) injection 30 minutes prior to the emetogenic chemotherapy, on day 1, by a healthcare professional; administer in combination with dexamethasone Due to the viscosity of the solution, injection should be administered over 20 to 30 seconds Do not administer more frequently than once every 7 days (effects last for ≈ 5 days); use > 6 months is not recommended Do not administer more frequently than once every 14 days in patients with moderate renal impairment (creatinine clearance [CrCl] 30-59 mL/min); avoid in patients with severe impairment (CrCl < 30 mL/min)	--	--	--	--	injection: 10 mg/0.4 mL extended-release injection in a single-dose, pre-filled syringe
ondansetron (Zofran, Zuplenz)	HEC: 24 mg (three -8 mg tabs) given 30 minutes before start of chemotherapy; MEC: 8 mg given 30 minutes before start of chemotherapy with a subsequent dose 8hours after the first dose; 8 mg should then be given every 12 hours for 1 to 2 days following completion of chemotherapy Injection: 0.15 mg/kg IV for 3 doses up to a maximum of 16 mg per dose The first dose is infused over 15 minutes starting 30 minutes before the start of chemotherapy; subsequent doses (0.15 mg/kg up to 16 mg per dose) are administered 4 and 8 hours after the first dose	HEC: No experience with 24 mg dosage MEC: 4-11 years: 4 mg given 30 minutes before chemotherapy with subsequent doses 4 and 8 hours after the first dose; 4 mg should be given every 8 hours for 1 to 2 days after completion of chemotherapy ≥ 12 years: same as adult. Injection: 6 months – 18 years: 0.15 mg/kg IV for 3 doses up to a maximum of 16 mg per dose; the first dose is given 30 minutes prior to moderately to HEC Subsequent doses (0.15 mg/kg IV up to a maximum of 16 mg per dose) are administered 4 and 8 hours after the first dose (infused over 15 minutes)	8 mg up to 2 hours before radiation and up to 3 times daily for 1 to 2 days	16 mg (two-8mg tabs) 1 hour before induction of anesthesia 4 mg IV over 2 to 5 minutes, immediately before induction of anesthesia or post-operatively if the patient did not receive prophylactic antiemetics and has N/V within 2 hours after surgery	1 month to 12 years: <40 kg: 0.1 mg/kg IV over 2 to 5 minutes > 40 kg: 4 mg IV over 2 to 5 minutes immediately prior to or following anesthesia induction or post-operatively if the patient did not receive prophylactic antiemetics and has N/V shortly after surgery	tablets: 4 mg, 8 mg oral soluble film (Zuplenz): 4 mg, 8 mg oral solution: 4 mg/5 mL orally disintegrating tablets (ODT): 4 mg, 8 mg injection: 2 mg/mL in 1 or 2 mL single-use vials or ampules (generic only) and 20 mL multi-dose vials prefilled syringe: 2 mg/1 mL in syringes containing 2 mL solution for injection: 16 mg per 50 mL or 100 mL (generic only)

Antiemetics Agents – Dosing & Availability

Drugs	Prevention of chemotherapy-induced N/V		Prevention of radiotherapy-induced N/V in adults or Other Use	Prevention of post-operative N/V		Availability
	Adult	Pediatric		Adult	Pediatric	
5-HT3 antagonists						
palonosetron (Aloxi)	A single 0.25 mg IV dose administered over 30 seconds Dosing should occur approximately 30 minutes prior to start of chemotherapy	Ages 1 month to < 17 years A single dose of 20 mcg/kg (up to 1.5 mg) administered over 15 minutes approximately 30 minutes prior to start of chemotherapy	--	A single 0.075 mg IV dose administered over 10 seconds immediately prior to the induction of anesthesia	--	injection: 0.25 mg/2 mL (generic only), 0.25 mg/5 mL single-use vials
Combination Products						
fosnetupitant/ palonosetron (Akynzeo)	1 vial (235 mg/0.25 mg) reconstituted in 50 mL (prepared as described in labeling) and administered as a 30-minute IV infusion approximately 30 minutes prior to the start of chemotherapy	--	--	--	--	injection: 235 mg fosnetupitant/ 0.25 mg palonosetron (as lyophilized powder for reconstitution) in single-dose vials
netupitant/ palonosetron (Akynzeo)	One 300/0.5 mg capsule administered approximately 1 hour prior to the start of chemotherapy as part of a regimen including dexamethasone	--	--	--	--	capsules: 300 mg netupitant/0.5 mg palonosetron

Antiemetics Agents – Dosing & Availability

Drugs	Prevention of chemotherapy-induced N/V		Prevention of radiotherapy-induced N/V in adults or Other Use	Prevention of post-operative N/V		Availability
	Adult	Pediatric		Adult	Pediatric	
Cannabinoids						
dronabinol (Marinol)	**Capsules (Marinol):** Anorexia in adult patients with AIDS – initial dose is 2.5 mg twice daily, 1 hour before lunch and dinner; the dosage can be reduced to 2.5 mg/day administered as a single dose of in the evening at bedtime; the dosage may be gradually increased to a maximum dose of 20 mg/day Chemotherapy-induced nausea and vomiting (CINV) – initial dose of 5 mg/m^2 given 1 to 3 hours prior to chemotherapy, then every 2 to 4 hours after chemotherapy for a total of 4 to 6 doses per day; the initial starting dose may be adjusted in increments of 2.5 mg/m^2 if necessary up to a maximum of 15 mg/m^2 (per dose)	--	--	--	--	Capsules: 2.5 mg, 5 mg, 10 mg
dronabinol (Syndros)	Anorexia in adult patients with AIDS – initial dose is 2.1 mg twice daily, 1 hour before lunch and dinner; maximum dose is 8.4 mg twice daily CINV – initial dose is 4.2 mg/m^2, 1 to 3 hours prior to chemotherapy, then every 2 to 4 hours after chemotherapy up to 4 to 6 doses per day; give first dose on an empty stomach; doses that follow can be given regardless of meals; however, dosing in relation to meal times should be kept consistent for each chemotherapy cycle (maximum dose is 12.6 mg/m^2) (can be administered via select silicone feeding tubes; see labeling for details)	--	--	--	--	Solution (Syndros): 5 mg/mL
nabilone (Cesamet)	Usual adult dose is 1 to 2 mg twice daily; 1 or 2 mg may be given the night prior to chemotherapy or 1 to 3 hours before initial chemotherapy; maximum daily dose of 6 mg in divided doses (3 times a day); the medication may be administered 2 or 3 times a day during the entire course of each chemotherapy cycle and for 48 hours after the last dose of each chemotherapy cycle	--	--	--	--	Capsules: 1 mg

Antiemetics Agents – Dosing & Availability

Drugs	Prevention of chemotherapy-induced N/V		Prevention of radiotherapy-induced N/V in adults or Other Use	Prevention of post-operative N/V		Availability
	Adult	Pediatric		Adult	Pediatric	
Antihistamines						
metoclopramide (Reglan)	1 to 2 mg/kg IV 30 minutes before chemotherapy and repeated every 2 hours for 2 doses, then every 3 hours for 3 doses	--	Relief of symptomatic GERD: 10 mg to 15 mg orally up to 4 times daily at least 30 minutes prior to eating and at bedtime for up to 12 weeks Relief of symptoms associated with diabetic gastroparesis: 10 mg IV, IM or orally 4 times daily at least 30 minutes prior to eating and at bedtime for 2 to 8 weeks; therapy should not exceed 12 weeks Facilitation of intestinal intubation or as a diagnostic aid in gastrointestinal radiography- 10 mg IV in a single dose	10 mg to 20 mg IM or IV near the end of surgery. Repeat every 4 to 6 hours as necessary; if required, a 20 mg dose may be used	--	tablets: 5 mg, 10 mg orally disintegrating tablets: 5 mg, 10 mg (generic only) solution: 5 mg/5 mL (generic only) injection: 5 mg/mL in 2 mL single-use vials or syringes (generic only)
Antihistamines						
doxylamine/ pyridoxine (Diclegis)	--	--	Nausea and vomiting of pregnancy: initially, take 2 tablets orally at bedtime; if symptoms persist, take an additional tablet in the morning on day 3; if symptoms persist, take an additional tablet mid-afternoon on day 4 (maximum dose 4 tablets per day)	--	--	Delayed-release tablets: 10 mg doxylamine/ 10 mg pyridoxine
doxylamine/ pyridoxine (Bonjesta)	--	--	Nausea and vomiting of pregnancy: initially (day 1), take 1 tablet orally at bedtime; on day 2 if symptoms persist, take an additional tablet in the morning (maximum dose 2 tablets per day)	--	--	Extended-release tablets: 20 mg doxylamine/ 20 mg pyridoxine

Antiemetics Agents – Dosing & Availability

Drugs	Prevention of chemotherapy-induced N/V		Prevention of radiotherapy-induced N/V in adults or Other Use	Prevention of post-operative N/V		Availability
	Adult	Pediatric		Adult	Pediatric	
Others						
phosphorated carbohydrate solution (Emetrol OTC)	--	--	Relief of upset stomach associated with nausea: ages 2 to < 12 years: 1 to 2 teaspoons age > 12 years: 1 to 2 tablespoons May repeat dose every 15 minutes or until distress subsides; should not be taken for more than 1 hour (5 doses)	--	--	oral solution: 3.74 g total sugar + 21.5 mg phosphoric acid per 5 mL
trimethobenzamide (Tigan)	--	--	Nausea and vomiting - 250 or 300 mg capsule: 3 to 4 times daily or 200mg IM 3 to 4 times daily The suppository formulation has not been proven effective for nausea and vomiting	--	--	injection: 100 mg/mL in 2 mL single-use vials and 20 mL multi-dose vials (Tigan only) capsules: 300 mg

Antivertigo Agents – Dosing & Availability

Drugs	Adult	Pediatric	Availability
Anticholinergics			
scopolamine (Transderm Scop)	N/V: SC injection: 0.6 to 1 mg Motion sickness: Transdermal: 1 disc applied behind the ear 4 hours prior to antiemetic need; disc may stay in place for up to 3 days (If repeat dose needed, apply to skin behind opposite ear) Oral: 250 to 800 mcg 1 hour prior to need for antiemetic	N/V: SC injection: 0.006 mg/kg	injection: 0.4 mg/mL in 1 mL vials transdermal: 1.5 mg per 72 hours (delivers 1 mg over 72 hours) (all Rx only)
Phenothiazines			
prochlorperazine (Compazine, Compro)	Immediate release tablets: 5 to 10 mg 3 to 4 times daily Sustained release capsules: 10 or 15 mg every 12 hours Rectal suppositories: 25 mg twice daily IV or IM: 5 to 10 mg repeated every 3 to 4 hours as needed (max dose is 40 mg/day)	Oral or rectal: Children 2 to 12 years (weight 18 to 39 kg): 2.5 mg 3 times per day or 5 mg twice per day (max: 15 mg/day) Children 2 to 12 years (weight 14 to 17 kg): 2.5 mg 2 to 3 times per day (max: 10 mg/day) Children 2 to 12 years (weight 9 to 13 kg): 2.5 mg once or twice per day (max: 7.5 mg/day) Children < 2 years of age and infants (weight < 9 kg): Dosage not established IV or IM: Children 2 to 12 years (weight 18 to 39 kg): 0.132 mg per kg deep IM injection given 3 to 4 times per day, not to exceed 10 mg per day on the first day of treatment (max: 15 mg per day on subsequent days) Children 2 to 12 years (weight 14 to 17 kg): 0.132 mg per kg deep IM injection given 3 to 4 times per day (max: 10 mg per day) Children 2 to 12 years (weight 9 to 13 kg): 0.132 mg per kg deep IM injection given 3 to 4 times per day (max: 7.5 mg per day) Children < 2 years and infants (weight < 9 kg): Dosage not established	tablets: 5 mg, 10 mg suppositories: 25 mg injection: 5 mg/mL in 2 mL and 10 mL vials (all Rx only)
promethazine (Phenergan)	Motion Sickness: Adults: 25 mg (oral or rectal) 30 to 60 minutes prior to departure, then every 12 hours as needed N/V: Adults: 12.5 to 25 (oral, rectal, IV, IM) mg every 4 to 6 hours as needed	Motion Sickness: Children > 2 years of age: 12.5 to 25 mg (oral or rectal) twice daily as needed with first dose given 30 to 60 minutes prior to departure N/V: Children > 2 years of age: 0.5 mg per pound (oral or rectal), max 25 mg per dose, every 4 to 6 hours as needed Children > 2 years of age: 6.25 to 12.5 mg (IM or IV) every 4 to 6 hours as needed (max: 25mg/dose)	tablets: 12.5 mg, 25 mg, 50 mg oral solution: 6.25 mg/5 mL suppositories: 12.5 mg, 25 mg, 50 mg injection: 25 mg/mL, 50 mg/mL in 1 mL ampules or vials (all Rx only)

Antivertigo Agents – Dosing & Availability

Drugs	Adult	Pediatric	Availability
Antihistamines			
dimenhydrinate (Dramamine, Motion Sickness)	Adults and children ≥ 12 years old: Oral: 1 to 2 tablets every 4 to 6 hours (do not exceed 8 tablets in 24 hours) Injection: 50 to 100 mg IM or IV every 4 hours (do not exceed 300 mg in 24 hours)	Children ages 6 to 12 years: Oral: ½ to 1 tablet every 6 to 8 hours (do not exceed 3 tablets in 24 hours) Children ages 2 to 6 years: Oral: ¼ to ½ tablet every 6 to 8 hours (do not exceed more than 1.5 tablets in 24 hours) Children ages 2 to 12 years: Injection: 1.25 mg/kg or 37.5 mg/m2 BSA IM or IV every 6 hours (do not exceed 300 mg in 24 hours)	tablets: 50 mg (OTC) chewable tablets: 25 mg, 50 mg (OTC) injection: 50 mg/mL in 1 mL multi-dose vials (Rx)
diphenhydramine (Benadryl)	Injection: 10 mg IV or IM initially then 20 to 50 mg every 2 to 3 hours as needed (do not exceed 400 mg in 24 hours) Oral: 25 to 50 mg every 4 to 6 hours in adults and children ages ≥12 years old (do not to exceed 300 mg in 24 hours)	Ages 6 to 12 years: Injection: 1 to 1.5 mg per kg IV or IM every 6 hours, not to exceed 300 mg per day Ages 6 to 12 years: Oral: 12.5 mg to 25 mg every 4 to 6 hours (do not exceed 150 mg in 24 hours) Ages < 6 years: Oral and injection: safety and efficacy have not been established	tablets: 25 mg, 50 mg (OTC) capsules: 25 mg, 50 mg (OTC) softgels/gelcaps: 25 mg (OTC) chewable tablet: 12.5 mg, 25 mg (OTC) injection: 50 mg/mL in 1 mL single-use vials and 10 mL multi-dose vials (Rx) oral dissolving film: 12.5 mg, 25 mg (OTC) oral dissolving tablet: 12.5 mg, 25 mg (OTC) oral solution: 12.5 mg/5 mL (OTC and Rx), 50 mg/30 mL (OTC) oral drops: 6.25 mg/mL (OTC)
meclizine (Bonine, Dramamine Less Drowsy)	Motion Sickness: Adults and children ≥ 12 years old (OTC Dramamine Less Drowsy): 25 to 50 mg taken 1 hour prior to travel; may repeat dose every 24 hours as needed Vertigo: Adults and children ≥ 12 years old: 25 to 100 mg daily in divided doses	--	chewable tablets: 25 mg (OTC) tablets: 12.5 mg (OTC), 25 mg (Rx and OTC)

Magellan Rx MANAGEMENT℠

Magellan Medicaid Administration

Substance Use Disorder (Opiate Dependence)

Opiate Dependence Treatments – Dosing & Availability

Drugs	Dosing	Availability
buprenorphine SL tablets	**For the treatment of opioid dependence induction:** –For patients dependent on short-acting opioid products or heroin in opioid withdrawal, the first dose should be administered when objective signs of moderate opioid withdrawal appear and not less than 4 hours after patient last used opioid –For patients dependent on long-acting opioid products and/or methadone, the first dose should be administered when objective signs of moderate opioid withdrawal appear and not less than 24 hours after the patient last used opioid –Adults and Adolescents ≥ 16 years: 8 mg buprenorphine sublingually on day 1, 16 mg buprenorphine sublingually on day 2, and then the patient should begin maintenance treatment; dosage titration over 2 days rather than 3 to 4 days appears to result in greater treatment success **For opioid dependence maintenance:** When used for maintenance dosing, adjustments should be made in increments or decrements of 2 to 4 mg to a dose that maintains a level of treatment which suppresses opioid withdrawal; the general range of buprenorphine maintenance dose is 4 mg to 24 mg per day; doses beyond this have not shown any clinical advantage; patients may require treatment indefinitely and should continue for as long as the patient continues to benefit	2 mg, 8 mg sublingual tablets
buprenorphine extended-release injection (Sublocade)	**For the treatment of moderate to severe opioid use disorder in patients following induction and dose adjustment with a transmucosal buprenorphine-containing product for a minimum of 7 days:** –300 mg SC injection monthly for 2 months followed by maintenance dosing of 100 mg SC injection monthly –The maintenance dose may be increased to 300 mg SC injection monthly for patients who tolerate the 100 mg injection but do not demonstrate a clinical response –No less than 26 days between doses Injections are administered by a healthcare provider (HCP) into the subcutaneous tissue in the abdomen no more frequently than every 26 days - see package insert for specifics regarding administration procedure	100 mg/0.5 mL, 300 mg/1.5 mL prefilled syringe with safety needle

Opiate Dependence Treatments – Dosing & Availability

Drugs	Dosing	Availability
buprenorphine implant, subdermal (Probuphine)	**For the maintenance treatment of opioid dependence in patients who have achieved and sustained prolonged clinical stability on low-to-moderate doses of a transmucosal buprenorphine-containing product:** 4 implants inserted subdermally by an HCP in the inner upper arm and retained in place for 6 months (remove by the end of 6 months; – insertion site should be evaluated 1 week after placement; visit schedule frequency should be no less than once-monthly for continued counseling and psychosocial support; if spontaneous expulsion occurs, patients should see provider promptly – If additional supplemental transmucosal buprenorphine doses are needed after implant is placed, patient should be seen and evaluated promptly; do not provide patients with as-needed buprenorphine-containing products; alternatives to the buprenorphine implant should be considered for patients requiring ongoing supplemental transmucosal buprenorphine during implant use – May repeat treatment for 1 additional treatment course (total of 12 months) by inserting a new set of 4 implants into opposite arm; if this cannot be done on the same day as removal, maintain treatment with previous transmucosal buprenorphine dosage following removal until new implants are placed; If additional treatment is needed following two, 6-month implants, transition patient back to transmucosal buprenorphine	Implant kit: 4-sterile implants containing 74.2 mg (equivalent to 80 mg of buprenorphine HCl; 26 mm by 2.5 mm) and 1 disposable applicator
buprenorphine/ naloxone buccal film (Bunavail)	**For the induction of opioid agonist dependence treatment:** – For patients dependent on short-acting opioid products or heroin in opioid withdrawal: ○ Day 1: initial dose of 2.1/0.3 mg, repeat in 2 hours (total up to 4.2/0.7 mg) ○ Day 2: up to 8.4/1.4 mg as a single dose – To avoid precipitating withdrawal syndrome, the first dose should be started when objective signs of moderate withdrawal appear (not less than 6 hours after the last used opioids) – For patients dependent on long-acting opioid products and/or methadone the recommended treatment is sublingual buprenorphine monotherapy due to the higher risk of precipitated and prolonged withdrawal; after induction, patients can then be transitioned to once daily Bunavail buccal film – Additional titration details are outlined in the prescribing information **For the maintenance treatment of opioid dependence in patients who have been initially inducted using buprenorphine sublingual tablets:** – From Day 3 onward; dose adjustments should be made in increments/decrements of 2.1/ 0.3 mg to a level that suppresses opioid withdrawal symptoms; recommended target daily dose: 8.4/1.4 mg daily (single dose) – Maintenance dose range: 2.1/0.3 mg to 12.6/2.1 mg daily; higher doses have not shown any clinical advantage; no more than 2 films should be applied to 1 cheek at a time; patients may require treatment indefinitely and should continue for as long as the patient continues to benefit – If the patient is switching from Suboxone sublingual tablets, the equivalency chart in the package insert should be followed; a Bunavail 4.2/0.7 mg buccal film provide equivalent exposure to a Suboxone 8/2 mg sublingual film	2.1/0.3 mg, 4.2/0.7 mg, 6.3/1 mg buccal films (citrus flavor)

Opiate Dependence Treatments – Dosing & Availability

Drugs	Dosing	Availability
buprenorphine / naloxone SL film (Suboxone)	**For the induction of opioid agonist dependence treatment:** – For patients dependent on short-acting opioid products or heroin in opioid withdrawal: o Day 1: initial dose of 2/0.5 mg or 4/1 mg; may titrate upwards in 2 mg to 4 mg increments of buprenorphine, at 2 hour intervals to maximum of 8/2 mg o Day 2: up to 16/4 mg as a single dose – To avoid precipitating withdrawal syndrome, the first dose should be started when objective signs of moderate withdrawal appear; not less than 6 hours after the last used opioids – For patients dependent on long-acting opioid products and/or methadone: recommended treatment is sublingual buprenorphine monotherapy on Days 1 and 2; after induction, patients can then be transitioned to once daily sublingual film – Additional titration details are outlined in the prescribing information **For the maintenance treatment of opioid dependence::** – Titrate dosage in increments of 2–4 mg/day of buprenorphine to a dose that holds the patient in treatment and suppresses opioid withdrawal symptoms; doses above 24 mg/day have not shown any added benefit; an adequate maintenance dose, titrated to clinical effectiveness, should be achieved as rapidly as possible to avoid drop-out of patients during the induction period – Following induction to opioid dependence treatment, a target dose of 16/4 mg buprenorphine/naloxone sublingually once daily is suggested; however, doses ranging from 4 to 24 mg/day of the buprenorphine component may be required; patients may require treatment indefinitely and should continue for as long as the patient continues to benefit	2/0.5 mg, 4/1 mg, 8/2 mg, 12/3 mg sublingual films
buprenorphine / naloxone SL tablets (Zubsolv)	**For the induction of opioid agonist dependence treatment:** – For patients dependent on heroin or other short-acting opioid products: o Day 1: initiate with 1.4/0.36 mg, repeat at 1.5 to 2 hour intervals for a total daily dose up to 5.7/1.4 mg o Day 2: single dose up to 11.4/2.9 mg is recommended – May be induced on buprenorphine/naloxone SL tablets or with sublingual buprenorphine monotherapy; the dose should be initiated when moderate signs of opioid withdrawal appear (not less than 6 hours after the patient last used opioids) – For patients dependent on long-acting opioid products and/or methadone: recommended treatment is sublingual buprenorphine monotherapy on Days 1 and 2; after induction, patients can then be transitioned to once daily sublingual tablet – Additional titration details are outlined in the prescribing information **For the maintenance of opioid agonist dependence treatment:** – Titrate dose in increments of 1.4/0.36 mg or 2.9/0.71 mg of buprenorphine/naloxone to a dose that holds the patient in treatment and suppresses opioid withdrawal symptoms; doses above 17.2/4.2 mg per day of buprenorphine/naloxone have not shown to provide any additional clinical benefit – Following induction to opioid dependence treatment, a target dose of 11.4/2.9 mg buprenorphine/naloxone is recommended; however, doses ranging from 2.9/0.71 mg buprenorphine/naloxone to 17.2/4.2 mg buprenorphine/naloxone may be required; patients may require treatment indefinitely and should continue for as long as the patient continues to benefit	0.7/0.18 mg, 1.4/0.36 mg, 2.9/0.71 mg, 5.7/1.4 mg, 8.6/2.1 mg, 11.4/2.9 mg sublingual tablets

Opiate Dependence Treatments – Dosing & Availability

Drugs	Dosing	Availability
buprenorphine / naloxone SL tablets	**For the maintenance of opioid agonist dependence treatment:** – Titrate dose in increments of 2/0.5 mg/day or 4/1 mg/day of buprenorphine/naloxone to a dose that holds the patient in treatment and suppresses opioid withdrawal symptoms; doses above 24/6 mg per day of buprenorphine/naloxone have not shown to provide additional clinical benefit – Following induction to opioid dependence treatment, a target dose of 16/4 mg buprenorphine/naloxone is recommended; however, doses ranging from 4/1 mg buprenorphine/naloxone to 24/6 mg buprenorphine/naloxone may be required; patients may require treatment indefinitely and should continue for as long as the patient continues to benefit	2/0.5 mg, 8/2 mg sublingual tablets
lofexidine (Lucemyra)	**For the mitigation of opioid withdrawal symptoms:** – Three 0.18 mg tablets 4 times daily during peak withdrawal symptoms (typically 5 to 7 days after last opioid); adjust dose based on symptoms and side effects maintaining 5 to 6 hours between each dose; maximum total daily dose 2.88 mg (16 tablets); maximum single dose is 0.72 mg (4 tablets) – Treatment may continue for up to 14 days based on opioid withdrawal symptoms; gradual dose reduction over 2 to 4 days is recommended to discontinue lofexidine to avoid withdrawal symptoms	0.18 mg tablets
naloxone hydrochloride injection (Evzio)	**Emergency treatment of opioid overdose, either known or suspected, as demonstrated by respiratory and/or central nervous system depression:** – Not intended as a substitute for emergency medical care but for immediate administration as emergency therapy when opioids may have been used – Dosage: 0.4 mg or 2 mg by intramuscular or subcutaneous injection only into the anterolateral aspect of the thigh of adult or pediatric patients, through clothing, if needed; for pediatric patients less than 1 year of age, the thigh muscle should be pinched while the dose is administered – If the voice instruction system does not operate properly, the intended dose of naloxone hydrochloride will still be delivered if the auto-injector is used according to printed instructions on the label Immediately after administration, emergency medical care should be sought; additional doses may be administered every 2 to 3 minutes until arrival of emergency medical assistance	2 mg/0.4 mL solution in a pre-filled auto-injector (supplied as 2 Evzio 2 mg auto-injectors and a single Trainer) 0.4 mg/mL, 2 mg/2 mL syringes (institutional use)* 0.4 mg/mL single-dose vials* 0.4 mg/mL multidose vials*
naloxone hydrochloride nasal spray (Narcan)	**Emergency treatment of opioid overdose, either known or suspected, as demonstrated by respiratory and/or central nervous system depression:** (Not intended as a substitute for emergency medical care but for immediate administration as emergency therapy when opioids may have been used) Administer 1 spray into a single nostril; may administer additional doses using a new nasal spray with each dose if there is no response or relapse occurs; additional doses may be administered every 2 to 3 minutes as needed until emergency assistance arrives	4 mg/0.1 mL nasal spray (supplied as 2 blister packages per carton, with each blister containing a single nasal spray)

Opiate Dependence Treatments – Dosing & Availability

Drugs	Dosing	Availability
naltrexone hydrochloride tablets	**Opioid dependence:** – Initiate after completion of opioid detoxification and a minimum 7 to 10 day opioid-free interval for patients previously using short-acting opioids; since absence of an opioid drug in the urine is not a sufficient indication that a patient is opioid-free, a naloxone challenge test may be administered; if the challenge test is positive, do not initiate therapy; repeat the test in 24 hours – Initial dose 25 mg daily; if no evidence of withdrawal, initiate 50 mg (doses as low as 12.5 mg have been used initially-titrating by 12.5 mg daily until 50mg dose has been achieved) – Supervised alternate dosing schedules may be required; 50 mg daily on weekdays with 100 mg on Saturday; 100 mg every other day; 150 mg every third day **Alcohol dependence:** 50 mg once daily (following verification that patient is opioid-free); safety and efficacy established only in short-term (up to 12 weeks of therapy)	50 mg tablets (scored)
naltrexone extended-release injectable suspension (Vivitrol)	**For the treatment of alcohol dependence in patients who are able to abstain from alcohol in an outpatient setting and for the prevention of relapse to opioid dependence following opioid detoxification:** – 380 mg intramuscularly by and HCP into the gluteal muscle every 4 weeks or once monthly; patients must be opioid-free a minimum of 7 to 10 days and should not be drinking alcohol at the time of therapy initiation	380 mg vial per 4 mL diluent

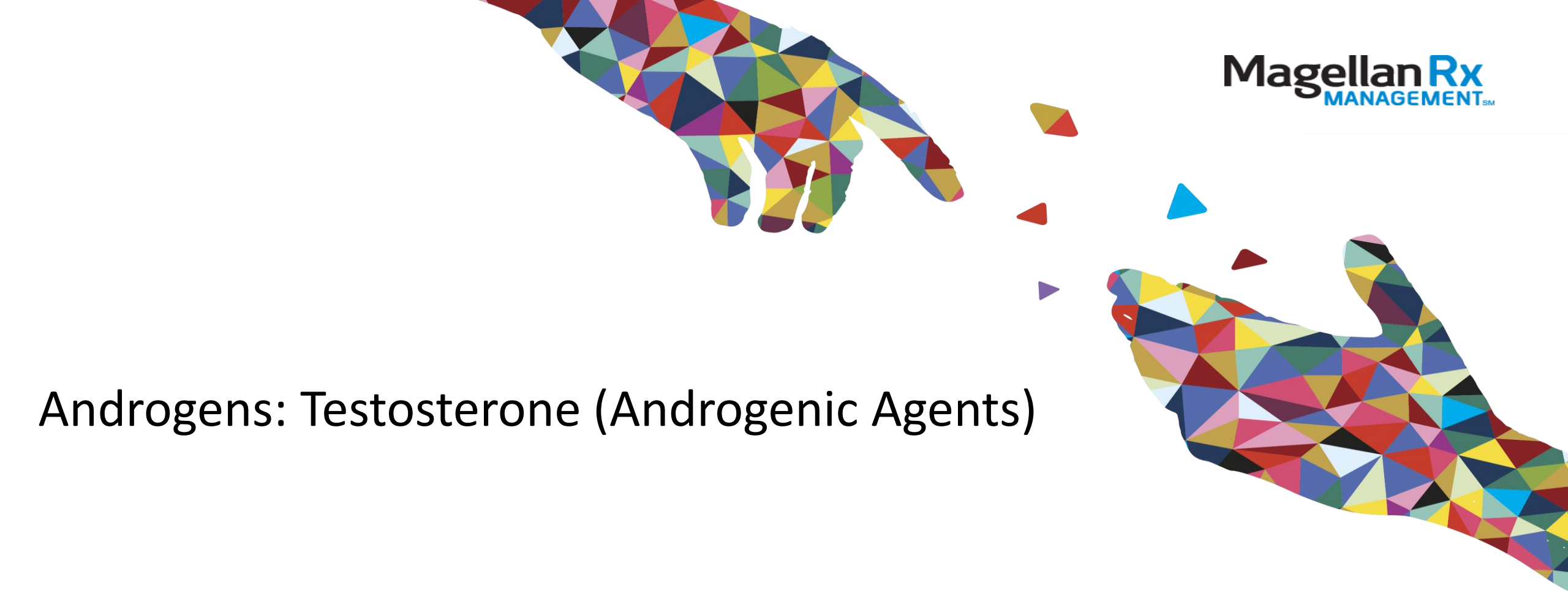
Magellan Rx MANAGEMENT℠

Magellan Medicaid Administration

Prostatic Hypertrophy Agents (BPH Agents)

Benign Prostatic Hyperplasia – Dosing & Availability

Drugs	Initial Dose for BPH	Maintenance Dose for BPH	Dosage Forms
Alpha-Blockers			
alfuzosin ER (Uroxatral)	10 mg daily	10 mg daily	10 mg extended-release tablets
doxazosin (Cardura)	1 mg daily	1 – 8 mg daily	1 mg, 2 mg, 4 mg, 8 mg tablets
doxazosin ER (Cardura XL)	4 mg daily	4 – 8 mg daily taken with breakfast	4 mg, 8 mg extended-release tablets
silodosin (Rapaflo)	8 mg daily Moderate renal impairment: 4 mg daily	8 mg daily Moderate renal impairment: 4 mg daily	4 mg, 8 mg capsules
tamsulosin (Flomax)	0.4 mg daily	0.4 – 0.8 mg daily	0.4 mg capsules
terazosin	1 mg daily	2 – 20 mg daily	1 mg, 2 mg, 5 mg, 10 mg capsules
5-Alpha Reductase (5AR) Inhibitors			
dutasteride (Avodart)	0.5 mg daily	0.5 mg daily	0.5 mg capsules
finasteride (Proscar)	5 mg daily	5 mg daily	5 mg tablets
5-Alpha Reductase (5AR) Inhibitors / Alpha-Blocker Combinations			
dutasteride/ tamsulosin (Jalyn)	1 capsule daily (0.5 mg dutasteride/0.4 mg tamsulosin)	1 capsule daily (0.5 mg dutasteride/0.4 mg tamsulosin)	0.5 mg dutasteride/ 0.4 mg tamsulosin per capsule
Phosphodiesterase 5 (PDE5) Inhibitors			
tadalafil (Cialis)	5 mg daily CrCl 30 – 50 mL/min: 2.5 mg daily	5 mg daily CrCl 30 – 50 mL/min: may increase to 5 mg daily based on individual response	2.5 mg, 5 mg, 10 mg, 20 mg tablets (10 mg and 20 mg strengths are not used in BPH)



Androgens: Testosterone (Androgenic Agents)

Magellan Medicaid Administration

Androgenic Agents – Current Product Listing

Androgenic Agents, Oral; Current Product Listing

LABEL NAME	MANUFACTURER	DRUG TYPE	PROVIDER SYNERGIES BRAND NAME ROUTE
ANADROL-50 TABLET	MEDA/MYLAN SPEC	SSB	ANADROL-50 (ORAL)
METHITEST 10 MG TABLET	IMPAX GENERICS	SSB	METHITEST (ORAL)
METHYLTESTOSTERONE 10 MG CAP	GLOBAL PHARM	GEN	METHYLTESTOSTERONE (ORAL)
OXANDROLONE 10 MG TABLET	generic	GEN	OXANDROLONE (ORAL)
OXANDROLONE 2.5 MG TABLET	generic	GEN	OXANDROLONE (ORAL)
STRIANT 30 MG MUCOADHESIVE	AUXILIUM/ENDO P	SSB	STRIANT (BUCCAL)