Magellan Rx MANAGEMENT℠

Magellan Medicaid Administration

Washington Pharmacy Advisory Committee Meeting

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Agenda Topics

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

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Psychotherapeutic and Neurological Agents: ADHD/ Anti-narcolepsy: Stimulants and Non-Stimulants

Overview of Disease State
ADHD/ Anti-narcolepsy: Stimulants and Non-Stimulants

- Attention Deficit Hyperactivity Disorder (ADHD)
  - ADHD, which has been diagnosed in approximately 15% of children 4 to 17 years of age and about 4% of adults, is a chronic condition with core symptoms of inattention, hyperactivity, and difficulty controlling behavior
  - It may also be accompanied by internalized disorders, such as sadness and anxiety, as well as aggressive and oppositional disorders
  - The 3 main types of ADHD are
    - Primary hyperactive
    - Primary inattentive
    - Mixed
  - Children with ADHD may experience:
    - Academic underachievement
    - Difficulties in personal relationships
    - Low self-esteem
  - Symptoms of ADHD tend to improve with age; however, this may be due in part to improved coping skills
    - The continuation of synaptogenesis and myelinization into adolescence and young adulthood (especially in the frontal lobes) may also play a role in the improvement of symptoms
    - One-third of children with ADHD will retain the diagnosis as they enter into adulthood

Overview of Disease State
ADHD/ Anti-narcolepsy: Stimulants and Non-Stimulants

- Hypersomnolence
  - Excessive sleepiness, or hypersomnolence, is the primary and often debilitating symptom experienced by patients with narcolepsy, obstructive sleep apnea-hypopnea syndrome (OSAHS), and shift work sleep disorder (SWSD)
  - The defining characteristic of hypersomnolence is a consistent inability to stay awake and alert enough to safely and successfully accomplish tasks of daily living
  - Persons experiencing excessive sleepiness who seek medical attention typically complain of fatigue, tiredness, lapses of attention, lack of energy, low motivation, difficulty concentrating, disrupted sleep, snoring, or difficulties at work
- Treatment
  - While continuous positive airway pressure (CPAP) therapy has been shown to improve daytime sleepiness in patients with obstructive sleep apnea (OSA), the level of sleepiness does not always normalize.
  - To address this residual daytime sleepiness, pharmacologic treatments may be beneficial in users of CPAP
  - Modafinil (Provigil), armodafinil (Nuvigil), and solriamfetol (Sunosi) are FDA-approved for excessive daytime sleepiness associated with OSAHS. Modafinil and armodafinil are also indicated for sleep problems resulting from circadian rhythm disruption (e.g., SWSD)
  - Modafinil, armodafinil, and solriamfetol, along with central nervous system (CNS) stimulants, such as dextroamphetamine (Dexedrine, Procentra, Zenzedi), methylphenidate (Methylin, Ritalin, Metadate ER), mixed amphetamine salts (Adderall), and amphetamine sulfate tablet (Evekeo), are used for narcolepsy
  - The potential for adverse cardiovascular events with CNS stimulant use may be of concern, especially in this overall high-risk patient population
  - Due to their lack of sympathomimetic activity, modafinil and armodafinil are relatively free of adverse cardiovascular effects

Guidelines ADHD/ Anti-narcolepsy: Stimulants and Non-Stimulants

- American Academy of Pediatrics (AAP), 2011
  - The primary care clinician should initiate an evaluation for ADHD for any child 4 through 18 years of age who presents with academic or behavioral problems and symptoms of inattention, hyperactivity, or impulsivity
  - The treatment of patients with ADHD should maximize function to improve relationships and performance at school, decrease disruptive behaviors, promote safety, increase independence, and improve self-esteem
  - Treatment
    - Recommends parent- and/or teacher-administered behavior therapy as first-line treatment for children 4 to 5 years of age
    - Methylphenidate (MPH) may be prescribed if the behavior interventions do not provide significant improvement and there continues to be moderate to severe disturbance in the child's function
    - For children 6 to 11 years of age, the evidence is particularly strong for stimulant medication use and sufficient, but less strong evidence, for atomoxetine, extended-release guanfacine, and extended-release clonidine; however, medication therapy in addition to behavioral therapy is recommended
    - For patients 12 to 18 years of age, the AAP recommends FDA-approved medications, with the adolescent's assent, and behavior therapy as treatment for ADHD, preferably both American Academy of Pediatrics

Guidelines
ADHD/ Anti-narcolepsy: Stimulants and Non-Stimulants

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

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

ADHD/ Anti-narcolepsy: Stimulants and Non-Stimulants – Indications

Drugs	Generic	ADHD			Narcolepsy (Age ≥ 6 years)	Other Indications
		Age 3–5 years	Age ≥ 6 years	Adults		
Stimulants: Immediate-Release						
amphetamine sulfate tablet (Evekeo)	X	X	X	--	X	Exogenous obesity age ≥ 12 years
amphetamine sulfate orally disintegrating tablet (ODT) (Evekeo ODT)	--	--	X	--	--	--
armodafinil (Nuvigil)	X	--	--	--	--	Excessive sleepiness associated with narcolepsy, OSA, and SWD for age ≥ 17 years
dexmethylphenidate IR (Focalin)	X	--	X	--	--	--
dextroamphetamine IR (Zenzedi)	X	X	X (≤ 16 years)	--	X	--
dextroamphetamine solution (Procentra)	X	X	X (≤ 16 years)	--	X	--
methamphetamine (Desoxyn)	X	--	X	--	--	Exogenous obesity in adults and adolescents ≥ 12 years
methylphenidate IR (Methylin, Ritalin)	X	--	X	--	X	--

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ADHD/ Anti-narcolepsy: Stimulants and Non-Stimulants – Indications

Drugs	Generic	ADHD			Narcolepsy (Age ≥ 6 years)	Other Indications
		Age 3–5 years	Age ≥ 6 years	Adults		
Stimulants: Immediate-Release (Continued)						
mixed amphetamine salts IR (Adderall)	X	X	X	--	X	--
modafinil (Provigil)	X	--	--	--	--	Excessive sleepiness associated with narcolepsy, OSA, and SWD for age ≥ 17 years
Stimulants: Extended-Release						
amphetamine ER (Adzenys ER Adzenys XR-ODT)	--	--	X	X	--	--
amphetamine ER (Dyanavel XR)	--	--	X	X	--	--
dexmethylphenidate ER (Focalin XR)	X	--	X	X	--	--
dextroamphetamine ER (Dexedrine)	X	--	X (≤ 16 years)	--	X	--
lisdexamfetamine dimesylate (Vyvanse)	--	--	X	X	--	Moderate to severe binge eating disorder in adults
methylphenidate ER	X	--	X	--	--	--

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ADHD/ Anti-narcolepsy: Stimulants and Non-Stimulants – Indications

Drugs	Generic	ADHD			Narcolepsy (Age ≥ 6 years)	Other Indications
		Age 3–5 years	Age ≥ 6 years	Adults		
Stimulants: Extended-Release						
methylphenidate ER (Adhansia XR)	--	--	X	X	--	--
methylphenidate ER (Aptensio XR)	--	--	X	X	--	--
methylphenidate ER (Cotempla XR-ODT)	--	--	X	--	--	--
methylphenidate ER (Jornay PM)	--	--	X	X	--	--
methylphenidate ER (Metadate ER, Ritalin SR®)	X	--	X	X	X	--
methylphenidate ER (Quillichew ER)	--	--	X	X	--	--
methylphenidate ER (Quillivant XR)	--	--	X	X	--	--
methylphenidate ER (Ritalin LA)	X	--	X	--	--	--
methylphenidate ER OROS (Concerta)	X	--	X	X	--	--
methylphenidate transdermal (Daytrana®)	--	--	X	--	--	--
mixed amphetamine salts ER (Adderall XR)	X	--	X	X	--	--
mixed amphetamine salts ER (Mydayis)	--	--	--	-- (≥ 13 years)	--	--

ADHD/ Anti-narcolepsy: Stimulants and Non-Stimulants – Dosing and Availability

Drug	Ages	Usual Initial Dosage	Maximum Dosage	Dosage Forms
Stimulants: Immediate-Release				
amphetamine sulfate (Evekeo, Evekeo ODT)	3–5 years (tablet only)	2.5 mg once daily	40 mg/day in 2 or 3 divided doses	Tablets: 5 mg, 10 mg Orally disintegrating tablets (ODT): 5 mg, 10 mg, 15 mg, 20 mg
	6–17 years	5 mg once or twice daily		
armodafinil (Nuvigil)	≥ 17 years	150 mg to 250 mg once daily in the morning	250 mg/day	Tablets: 50 mg, 150 mg, 200 mg, 250 mg
dexmethylphenidate (Focalin)	6–17 years	2.5 mg twice daily	10 mg twice daily	Tablets: 2.5 mg, 5 mg, 10 mg
dextroamphetamine IR (Zenzedi)	3–5 years	2.5 mg once daily	40 mg/day	Tablets: 5 mg, 10 mg Tablets (Zenzedi): 2.5 mg, 5 mg, 7.5 mg, 10 mg, 15 mg, 20 mg, 30 mg
	6–16 years	5 mg once or twice daily	40 mg/day in 2 or 3 divided doses	
dextroamphetamine solution (Procentra)	3–5 years	2.5 mg once daily	40 mg/day; initial dose upon wakening, additional 1-2 doses every 4 to 6 hours	Oral solution: 5 mg/5 mL
	6–16 years	5 mg once or twice daily	40 mg/day; initial dose upon wakening, additional 1-2 doses every 4 to 6 hours	
methamphetamine (Desoxyn)	6–17 years	5 mg once or twice daily	20 to 25 mg/day in 2 divided doses	Tablets: 5 mg
methylphenidate IR (Methylin, Ritalin)	6–17 years	5 mg twice daily	60 mg/day in 2 or 3 divided doses	Tablets: 5 mg, 10 mg, 20 mg Chewable tablets: 2.5 mg, 5 mg, 10 mg Oral solution: 5 mg/5 mL, 10 mg/5 mL
mixed amphetamine salts IR (Adderall)	3–5 years 6–17 years	2.5 mg once daily 5 mg 1 or 2 times daily	40 mg/day	Tablets: 5 mg, 7.5 mg, 10 mg, 12.5 mg, 15 mg, 20 mg, 30 mg
modafinil (Provigil)	≥ 17 years	200 mg once daily in the morning	400 mg/day	Tablets: 100 mg, 200 mg

ADHD/ Anti-narcolepsy: Stimulants and Non-Stimulants – Dosing and Availability

Drug	Ages	Usual Initial Dosage	Maximum Dosage	Dosage Forms
Stimulants: Extended-Release				
amphetamine ER (Adzenys ER, Adzenys XR-ODT)	6–17 years	6.3 mg once daily in the morning	6 to 12 years: 18.8 mg/day 13 to 17 years: 12.5 mg/day	ODT:3.1 mg, 6.3 mg, 9.4 mg, 12.5 mg, 15.7 mg, and 18.8 mg Suspension: 562.5 mg/450 mL (1.25 mg/mL)
	≥ 18 years	12.5 mg once daily in the morning	12.5 mg/day	
amphetamine ER (Dyanavel XR)	≥ 6 years	2.5 to 5 mg once daily in the morning	20 mg/day	Suspension: 1,160 mg/ 464 mL (2.5 mg/mL)
dexmethylphenidate ER (Focalin XR)	6–17 years	5 mg once daily	30 mg/day	Capsules: 5 mg, 10 mg, 15 mg, 20 mg, 25 mg, 30 mg, 35 mg, 40 mg
	≥ 18 years	10 mg once daily	40 mg/day	
dextroamphetamine ER (Dexedrine)	6–16 years	5 mg once daily	40 mg once daily	Capsules: 5 mg, 10 mg, 15 mg
lisdexamfetamine (Vyvanse)	≥ 6 years	30 mg daily in the morning	70 mg daily in the morning	Capsules: 10 mg, 20 mg, 30 mg, 40 mg, 50 mg, 60 mg, 70 mg Chewable tablets: 10 mg, 20 mg, 30 mg, 40 mg, 50 mg, 60 mg
methylphenidate ER (Adhansia XR)	≥ 6 years	25 mg once daily	Adults: 100 mg daily Pediatrics: 85 mg daily	Capsules: 25 mg, 35 mg, 45 mg, 55 mg, 70 mg, 85 mg
methylphenidate ER (Aptensio XR)	≥ 6 years	10 mg once daily	60 mg once daily	Capsules: 10 mg, 15 mg, 20 mg, 30 mg, 40 mg, 50 mg, 60 mg
methylphenidate ER (Cotempla XR-ODT)	≥ 6 years	17.3 mg once daily in the morning	51.8 mg once daily	Extended-release ODT: 8.6 mg, 17.3 mg, 25.9 mg
methylphenidate ER (Jornay PM)	≥ 6 years	20 mg once daily in the evening	100 mg once daily in the evening	Capsules: 20 mg, 40 mg, 60 mg, 80 mg. 100 mg
methylphenidate ER (generics of Metadate CD)	6–17 years	20 mg once daily, in the morning before breakfast	60 mg once daily, in the morning before breakfast	Capsules (generic only): 10 mg, 20 mg, 30 mg, 40 mg, 50 mg, 60 mg

ADHD/ Anti-narcolepsy: Stimulants and Non-Stimulants – Dosing and Availability

Drug	Ages	Usual Initial Dosage	Maximum Dosage	Dosage Forms
Stimulants: Extended-Release (Continued)				
methylphenidate ER (Metadate ER, Ritalin SR)	6–17 years	5 mg twice daily or equivalent (e.g., 10 mg once daily)	60 mg/day in 1 or 2 divided doses	Tablets: 10 mg (generic only), 20 mg
	≥ 18 years	20 to 30 mg daily		
methylphenidate ER (Quillichew ER)	≥ 6 years	20 mg once daily in the morning	60 mg/day	Chewable tablets: 20 mg, 30 mg, 40 mg (20 and 30 mg are scored; 40 mg is not scored)
methylphenidate ER (Quillivant XR)	≥ 6 years	20 mg once daily	60 mg once daily	Suspension for reconstitution: 300 mg/60 mL, 600 mg/120 mL, 750 mg/150 mL, 900 mg/180 mL (25 mg/5mL)
methylphenidate ER (Ritalin LA)	6–17 years	20 mg once daily	60 mg once daily	Capsules: 10 mg, 20 mg, 30 mg, 40 mg, 60 mg (generic only)
methylphenidate ER OROS (Concerta)	6–12 years	18 mg once daily	54 mg once daily	Tablets: 18 mg, 27 mg, 36 mg, 54 mg, 72 mg
	13–17 years	18 mg once daily	72 mg once daily (< 2 mg/kg/day)	
	18–65 years	18 or 36 mg once daily	72 mg once daily	
methylphenidate transdermal (Daytrana)	6–17 years	10 mg patch worn 9 hours daily	30 mg patch worn 9 hours daily	Patches: 10 mg, 15 mg, 20 mg, 30 mg per 9 hours
mixed amphetamine salts ER (Adderall XR)	6–17 years	10 mg once daily	30 mg once daily	Capsules: 5 mg, 10 mg, 15 mg, 20 mg, 25 mg, 30 mg
	≥ 18 years (adults)	20 mg once daily	20 mg once daily	
mixed amphetamine salts ER (Mydayis)	13-17 years	12.5 mg once daily in the morning upon awakening	25 mg once daily	Capsules: 12.5 mg , 25 mg, 37.5 mg, 50 mg
	≥ 18 years		50 mg once daily	

ADHD/ Anti-narcolepsy: Non-Stimulants – Indications, Dosing and Availability

Drugs	Generic	ADHD			Narcolepsy (Age ≥ 6 years)	Other Indications
		Age 3–5 years	Age ≥ 6 years	Adults		
Non-Stimulants						
atomoxetine (Strattera)	**X**	--	**X**	**X**	--	--
clonidine ER (Kapvay)	**X**	--	**X**	--	--	Treatment of ADHD as adjunct to stimulants
guanfacine ER (Intuniv)	**X**	--	**X**	--	--	Treatment of ADHD as adjunct to stimulants
solriamfetol (Sunosi)	--	--	--	--	**X (adults only)**	OSA (adults)§

Drug	Ages	Usual Initial Dosage	Maximum Dosage	Dosage Forms
Stimulants: Extended-Release				
atomoxetine (Strattera)	≥ 6 years and < 70 kg	0.5 mg/kg/day in 1 or 2 divided doses	1.4 mg/kg/day in 1 or 2 divided doses	Capsules: 10 mg, 18 mg, 25 mg, 40 mg, 60 mg, 80 mg, 100 mg
	≥ 6 years and >70 kg and adults	40 mg/day in 1 or 2 divided doses	100 mg/day given in 1 or 2 divided doses	
clonidine ER (Kapvay)	6–17 years	0.1 mg at bedtime	0.2 mg twice daily	Tablets: 0.1 mg
guanfacine ER (Intuniv)	6–17 years	1 mg once daily in the morning or evening	4 mg once daily in the morning or evening	Tablets: 1 mg, 2 mg, 3 mg, 4 mg
solriamfetol (Sunosi)	≥ 18 years	Narcolepsy: 75 mg once daily upon waking OSA: 37.5 mg once daily upon waking	Narcolepsy: 150 mg OSA: 150 mg	Tablets, functionally-scored: 75 mg, 150 mg

ADHD/ Anti-narcolepsy: Pitolisant HCl (Wakix®)

- **Indication**
  - A histamine-3 (H_3) receptor antagonist/inverse agonist, is indicated for the treatment of excessive daytime sleepiness (EDS) in adult patients with narcolepsy
- **Contraindications**
  - Patients with severe hepatic impairment
  - Pitolisant prolongs the QT interval, with a corrected QT (QTc) increase of 4.2 msec at the highest recommended dose
    - Its use should be avoided in patients with known QT prolongation or those using other medications that are known to prolong the QT interval
    - Likewise, pitolisant should be avoided in patients with a history of cardiac arrhythmias or those at risk for torsade de pointe or sudden death (e.g., congenital QT prolongation, hypokalemia, hypomagnesemia, symptomatic bradycardia)
    - Hepatic or renal impairment may increase the risk of QT prolongation
- **Dosage**
  - Recommended dosage is 8.9 mg (2 x 4.45 mg tablets) orally once daily for 1 week (week 1), then increase dosage to 17.8 mg once daily for another week (week 2), and the dose can be further increased to 35.6 mg (2 x 17.8 mg tablets) once daily thereafter (week 3 and beyond)
  - The recommended dose range is 17.8 mg to 35.6 mg once daily, based on tolerability. All doses should be administered in the morning upon wakening
  - Achievement of a clinical response may take up to 8 weeks
- **Availability**
  - Tablets are available as pitolisant HCl, although the dose is reported as pitolisant free base
  - Pitolisant HCl 5 mg and 20 mg tablets are equivalent to 4.45 mg and 17.8 pitolisant free base, respectively

ADHD/ Anti-narcolepsy: Pitolisant HCl (Wakix®)

- **Place in Therapy**
  - According to the American Academy of Sleep Medicine (AASM), CNS stimulants are the standard of care for EDS
  - Modafinil or armodafinil is preferred as the standard initial treatment due to the more favorable side effect profile and less addictive properties when compared to older stimulants
  - Second-line treatments include methylphenidate and amphetamine stimulants
    - Historically, these medications have been the most widely in clinical practice, but clinical evidence remains limited
  - Pitolisant (Wakix) offers an additional treatment option for the treatment of EDS with a novel mechanism of action
  - Furthermore, it lacks a controlled substance designation; however, its required dose adjustments in special populations and drug interactions, as well as the established role of stimulants for the treatment of EDS, may limit its use

Asthma and COPD Agents: Anti-asthmatic Monoclonal Antibodies – IL-5 Antagonists and IgE Antibodies

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Overview of Disease State
Anti-asthmatic Monoclonal Antibodies - IL-5 Agonists and IgE Antibodies

- Prevalence of asthma in the United States (U.S.) continues to rise
  - An estimated 7.7% of adults and 8.4% of children (25.2 million Americans) have asthma with approximately 10% to 20% in poor control
- The National Asthma Education and Prevention Program (NAEPP) has defined asthma as a chronic inflammatory disorder of the airways in which many cells and cellular elements play a role
- Asthma phenotypes have been identified by clinical and/or pathophysiological characteristics
- It has been established that eosinophils play a role in the inflammatory process of asthma and eosinophilic asthma is identified as a phenotype of asthma
- Generally, patients with eosinophilic asthma have severe disease with high eosinophil levels in the blood and sputum despite treatment with a glucocorticoid. Persistent levels of eosinophils in sputum may also be an indicator of disease severity

Overview of Disease State - Urticaria

- The prevalence of chronic urticaria (CU) is estimated to be 0.5% to 5% of the general population
- Typically, CU presents as pruritic edematous red wheals of variable size and shape with surrounding erythema
- Chronic urticaria is defined as episodic or daily hives lasting for 6 weeks or more that impairs quality of life
- The majority of cases of CU have an undetermined cause (idiopathic); however, infectious and autoimmune conditions can be associated with CU
- Chronic urticaria may be associated with presence of mononuclear cells (CD4+ Th1 and Th2 lymphocytes), eosinophils, neutrophils, basophils, mast cells, and activated macrophages

Overview of Disease State - Eosinophilic granulomatosis with polyangiitis

- Eosinophilic granulomatosis with polyangiitis (EGPA) (previously known as Churg-Strauss syndrome)
  - A systemic vasculitis of small-to-medium vessels, characterized by allergic rhinitis, asthma, and hypereosinophilia
  - EGPA is a rare disease state affecting 1 to 3 out of 100,000 patients, with a higher incidence of about 1 per 15,000 in patients with asthma
  - Onset may occur between 15 and 70 years of age, but diagnosis is typically made between 35 and 50 years of age
  - While the direct cause of the disease is unknown, HLA-DRB4 positivity may be a genetic risk factor
  - Symptoms can vary from mild to life-threatening
- Diagnosis
  - A diagnosis may be confirmed if in addition to vasculitis, patients also have at least 4 of the following features: asthma, eosinophilia, neuropathy, pulmonary infiltrates, paranasal sinus abnormalities, and eosinophilic vasculitis
  - Scoring systems to assess the severity of vasculitis and guide initial therapy in patients with EGPA include the 5-factor score (FFS) and the Birmingham Vasculitis Activity Score (BVAS)
    - FFS ranges from 0 to 2, and attributes a point for one of the following and 2 points if 2 or more of the following are met: age > 65 years, cardiac insufficiency, gastrointestinal involvement, renal insufficiency, and ear/nose/throat manifestations
    - BVAS has historically been used to a greater extent in research than clinical practice and includes general symptoms in addition to organ involvement It can range from 0 to 68 with 1 point being allotted for persistent symptoms and 2 points for new or worsening symptoms
- Guidelines
  - No US guidelines are currently available for the treatment of EGPA
  - As a consensus, EGPA that is not severe in nature is often treated with oral corticosteroids alone, and more than 90% of patients achieve remission
  - Initial therapy may also include cyclophosphamide for patients with severe, multi-organ disease
  - Patients with severe EGPA may be transitioned to maintenance therapy with azathioprine, methotrexate, or leflunomide; evidence supporting their use is limited
  - Other treatments include anti-IL-5 antibodies such as Nucala, immunoglobulins, interferon-alpha, rituximab, or inhaled glucocorticoids
  - Notably, Nucala is the only FDA-approved medication for this disease state

Immunomodulators, Asthma – Indications

Drugs	Indications
	Interleukin-5 (IL-5) Antagonists
benralizumab (Fasenra)	▪ Add-on maintenance treatment of patients with severe asthma aged ≥ 12 years, and with an eosinophilic phenotype
mepolizumab (Nucala)	▪ Add-on maintenance treatment of patients with severe asthma aged ≥ 12 years, and with an eosinophilic phenotype ▪ The treatment of adult patients with eosinophilic granulomatosis with polyangiitis (EGPA)
reslizumab (Cinqair)	▪ Add-on maintenance treatment of patients with severe asthma aged ≥ 18 years, and with an eosinophilic phenotype
	Anti-Immune Globulin E (IgE) Antibody
omalizumab (Xolair)	• Moderate to severe persistent asthma in patients ≥ 6 years of age with a positive skin test or in vitro reactivity to a perennial aeroallergen and symptoms that are inadequately controlled with inhaled corticosteroids • Chronic idiopathic urticaria in adults and adolescents ≥ 12 years of age who remain symptomatic despite H1 antihistamine treatment

Immunomodulators, Asthma – Dosing and Availability

Drugs	Dose	Dosage/Administration Comments	Dosage Forms
Interleukin-5 (IL-5) Antagonists			
benralizumab (Fasenra)	30 mg subcutaneously (SC) every 4 weeks for 3 doses, followed by 30 mg once every 8 weeks thereafter	For SC use only (upper arm, thigh, abdomen) Should only be administered by an HCP	30 mg/mL solution in a single-dose prefilled syringe
mepolizumab (Nucala)	**Asthma**: 100 mg SC every 4 weeks **EPGA**: 300 mg SC every 4 weeks as 3 separate 100 mg injections spaced at least 5 cm apart	For SC use only (upper arm, thigh, abdomen) The vial for reconstitution should only be administered by an HCP The prefilled autoinjector and prefilled syringe can be administered by the patient or a caregiver; the SC injection can be given in the thigh, abdomen, or upper arm	100 mg lyophilized powder for injection in a single-dose vial 100 mg/mL solution in a SDP autoinjector and SDP syringe
reslizumab (Cinqair)	3 mg/kg every 4 weeks by intravenous (IV) infusion over 20 to 50 minutes	For IV infusion only; do not administer vial IV push or bolus. Should only be administered in a healthcare setting by an HCP who can manage anaphylaxis Discontinue infusion immediately if anaphylaxis occurs	100 mg/10 mL solution in single-use vial
Anti-Immune Globulin E (IgE) Antibody			
omalizumab (Xolair)	**Asthma:** 75 mg to 375 mg SC every 2 or 4 weeks Dose and frequency is determined by serum total IgE level before the start of treatment, and body weight, as instructed in the package insert **CIU:** 150 mg to 300 mg SC every 4 weeks Dosing is not dependent on serum IgE or body weight	Should only be administered in a healthcare setting by an HCP who can manage anaphylaxis Injection may take 5 to 10 seconds to administer due to the solution viscosity Doses > 150 mg should be divided among more than one injection site; do not administered > 150 mg per site	150 mg lyophilized powder for injection in a single-dose vial 75 mg/0.5 mL and 150 mg/1 mL solution in a SDP syringe

Immunomodulators, Asthma – Guidelines

- American Thoracic Society (ATS) and European Respiratory Society (ERS) Task Forces, 2014
  - Severe asthma defined as asthma that requires treatment with high-dose inhaled corticosteroids (ICS) plus a second controller and/or systemic corticosteroids to prevent it from becoming uncontrolled or that remains uncontrolled despite this therapy
  - The guidelines suggest a trial of omalizumab (Xolair) in adults and children aged 6 years and older with a confirmed IgE-dependent allergic asthma despite optimal drug and non-drug therapy
  - If there is no response within 4 months of beginning omalizumab, it is unlikely that continued treatment will be of benefit
  - Benralizumab (Fasenra), mepolizumab (Nucala), and reslizumab (Cinqair) were not available at the time that these guidelines were published

Immunomodulators, Asthma – Guidelines

- Global Initiative for Asthma (GINA), 2019
  - Offer a management plan to adjust treatment in a continuous cycle of assessment, treatment, and review of the patient's response as it relates to symptom control, future risk of exacerbations, and side effects
  - During this continuous cycle, a stepwise treatment approach is used to achieve control using the patient's current level of control as the baseline
    - If the patient is not controlled on the current regimen, treatment should be stepped up until control is achieved
  - According to GINA's stepwise approach, patients in steps 1 and 2 are considered to have mild asthma, patients in step 3 to 4, moderate asthma, and patients in steps 4 and 5, moderate to severe asthma
  - The 2019 GINA guidelines recommend that all adults and adolescents with asthma receive an ICS-containing controller medication
  - Due to the increased risk of severe exacerbations and asthma-related death, short-acting beta agonist (SABA)-only treatment is no longer recommended
  - For most asthma patients, treatment can be initiated with an as-needed low dose ICS-formoterol (step 1) or daily low dose ICS (step 2)
  - In patients whose asthma is uncontrolled on a low-dose ICS-containing controller despite good adherence and correct technique, a step up in treatment may be added (see tables on next slide)
    - Any step up in therapy should be re-assessed after 2 to 3 months; if there is not an adequate response, consider alternative treatment options or a referral
    - If asthma control is maintained for at least 3 months on the current regimen, treatment can be stepped down to the lowest step and dosage that maintains control

Immunomodulators, Asthma – Guidelines

- Global Initiative for Asthma (GINA), 2019
  - Severe asthma is uncontrolled asthma despite adherence with optimized step 4 or step 5 treatment, correct inhaler technique, and proper management of contributory factors or asthma that worsens when high dose therapy is decreased
  - If asthma is uncontrolled after 3 to 6 months on high dose ICS-LABA, it is recommended to refer to a specialist and phenotype into categories, such as severe allergic, aspirin-exacerbated, or eosinophilic asthma, as this may guide the selection of add-on treatment
    - Add-on treatments for severe asthma include tiotropium (Spiriva), low-dose azithromycin (off-label), a leukotriene receptor antagonist (LTRA), a monoclonal antibody (benralizumab [**Fasenra**], mepolizumab [**Nucala**], omalizumab [**Xolair**], dupilumab [**Dupixent**]), a low-dose oral corticosteroid (OCS), bronchial thermoplasty, or sputum-guided therapy
      - Patients with severe allergic asthma with elevated immunoglobulin E (IgE) levels may benefit from Xolair (anti-IgE) therapy (Evidence A)
      - Those with severe eosinophilic asthma may benefit from Fasenra, Nucala, and Cinqair (anti-IL-5) therapy (Evidence A)
      - Those with severe eosinophilic/Type 2 asthma or patients requiring maintenance OCS may benefit from Dupixent (anti-IL-4) therapy (Evidence A)
      - Those with aspirin sensitivity may benefit from leukotriene receptor antagonists (LTRA) (Evidence B)

Immunomodulators, Asthma – Guidelines

- Global Initiative for Asthma (GINA), 2019 – Controller Therapy

Step	Age Group	Preferred Controller	Other Controller Options
Step 1: Symptom-driven or regular controller	≥ 12 years	▪ As-needed low dose ICS-formoterol (unlabeled indication)	▪ Low dose ICS whenever SABA is taken (unlabeled indication)
	6 to 11 years	--	▪ Low dose ICS whenever SABA is taken (unlabeled indication) or daily low dose ICS
Step 2: One controller AND an as-needed reliever medication	≥ 12 years	▪ Low dose ICS or as needed low dose ICS-formoterol (unlabeled indication)†	▪ Leukotriene modifier or low dose ICS whenever SABA is taken (unlabeled indication)
	6 to 11 years	▪ Low dose ICS	▪ Leukotriene modifier or low dose ICS whenever SABA is taken (unlabeled indication)
Step 3: Two controllers and an as-needed reliever medication	≥ 12 years	▪ Low dose ICS/LABA	▪ Medium dose ICS OR low dose ICS + leukotriene modifier ▪ Sublingual immunotherapy (SLIT) may be considered in adults with allergic rhinitis, house dust mite sensitivity, and FEV > 70% predicted
	6 to 11 years	▪ Low dose ICS/LABA or medium dose ICS	▪ Low dose ICS + leukotriene modifier

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Immunomodulators, Asthma – Guidelines

- Global Initiative for Asthma (GINA), 2019 – Controller Therapy

Step	Age Group	Preferred Controller	Other Controller Options
Step 4: Two controllers and an as-needed reliever medication	≥ 12 years	▪ Medium dose ICS/LABA	▪ High dose ICS, add-on tiotropium, or add-on leukotriene modifier ▪ Sublingual immunotherapy (SLIT) may be considered in adults with allergic rhinitis, house dust mite sensitivity, and FEV > 70% predicted
	6 to 11 years	▪ Medium dose ICS/LABA; refer for expert advice	▪ High dose ICS/LABA, add-on tiotropium, or add-on leukotriene modifier
Step 5: Two controllers and an as-needed reliever medication	≥ 12 years	▪ High dose ICS/LABA; refer for phenotypic assessment with or without add-on therapy (e.g., tiotropium, anti-IgE [omalizumab], anti-interleukin-5[IL5]/5R [mepolizumab, reslizumab, benralizumab], anti-IL4R [dupilumab])	▪ Add-on low dose oral corticosteroid, considering adverse effects
	6 to 11 years	▪ **Refer for phenotypic assessment with or without add-on therapy (e.g., anti-IgE [omalizumab)**	▪ **Add-on anti-IL-5 or add-on low dose oral corticosteroid, considering adverse effects**

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Immunomodulators, Asthma – Guidelines

- Global Initiative for Asthma (GINA), 2019 – Reliever Therapy

Step	Age Group	Preferred Reliever	Other RelieverOptions
≥ 12 years	Steps 1 and 2	▪ As-needed low dose ICS-formoterol (unlabeled indication)	▪ As needed SABA
	Steps 3 through 5	▪ As-needed low dose ICS-formoterol (unlabeled indication)	
6 to 11 years	Steps 1 through 5	▪ As needed SABA	--

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Immunomodulators, Urticaria – Guidelines

- The AAAAI/ACAAI/JCAAI recommend a stepwise approach to care is recommended for chronic urticaria
- Treatment should begin based on the patient's level of severity and previous treatment history
- At each level, medications should be evaluated for efficacy and patient tolerance and step-down should be considered when consistent control is achieved
- Step 1:
  - Monotherapy with second-generation antihistamines is considered first-line for CU in addition to avoidance of triggers (e.g., nonsteroidal anti-inflammatory drugs, food allergens) and relevant physical factors
- Step 2:
  - If CU is not controlled, the antihistamine dose can be increased (if appropriate for the particular agent)
  - One of the following can be added: another second-generation or a first-generation antihistamine, a histamine-2 antagonist, or an LTRA
- Step 3
  - If control is still not achieved, dose advancement of a potent antihistamine (e.g. hydroxyzine or doxepin) may be considered, as tolerated
- Step 4:
  - CU that is refractory to maximal antihistamine therapy in step 3, alternative agents such as Xolair (omalizumab) can be used; other anti-inflammatory, immunosuppressant, or biologic agents may be considered, but have a lower level of supporting evidence

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Magellan Medicaid Administration

Atopic Dermatitis Agents: Topical Immunosuppressives

Overview of Disease State
Atopic Dermatitis Agents: Topical Immunosuppressives

Atopic dermatitis (AD)

- A chronic, non-contagious, inflammatory disease of the skin resulting from a combination of genetic and environmental factors
- Often referred to as “eczema,” AD affects up to 25% of children and about 2% to 3% of adults
  - ~ 70% of patients diagnosed with AD have a positive family history of atopic diseases
  - Odds of developing AD are 2-3 times higher in children with one atopic parent and increase to 3 to 5 times higher if both parents are atopic
- Although symptoms of AD can develop at any age, it has been estimated that 60% of patients develop symptoms in the first year of life, while 90% develop symptoms before the age of 5 years
  - Majority of affected patients have resolution of the disease by adulthood, 10% to 30% do not, and a smaller percentage first develops symptoms as adults
  - Onset after age 30 years is less common and is often caused by exposure of the skin to harsh or wet conditions
  - AD commonly occurs in patients affected by asthma and other allergic conditions and is associated with elevated serum IgE levels
  - People who reside in cities and in dry climates appear to be more likely to develop this condition
  - AD is characterized by extremely dry, itchy skin on the insides of the elbows, behind the knees, and on the face, hands, and feet
- In response to the intense itching, patients may scratch or rub the affected area, which leads to further irritation and inflammation
  - As the skin loses moisture from the epidermal layer, it becomes increasingly dry and may begin to crack, weep, crust, and scale
  - This damage to the integrity of the skin renders it less protective and more prone to infection. Despite the chronic nature of this dermatologic condition, there may be periods of the disease when the skin improves and periods when the skin worsens
  - Irritants, such as detergents, fumes, tobacco smoke, and alcohol-containing skin products, and allergens like dust mites, pollen, and animal dander can exacerbate AD or cause “flare ups”

Atopic Dermatitis Agents: Topical Immunosuppressives – Indications

Drugs	Generic	FDA-Approved Indications
crisaborole (Eucrisa)	--	Topical treatment of mild to moderate atopic dermatitis in patients 2 years of age and older
dupilumab (Dupixent)	--	Treatment of patients 12 years and older with moderate to severe atopic dermatitis whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable; may be used with or without topical corticosteroids
pimecrolimus (Elidel)	**X**	Second-line therapy for the short-term and non-continuous chronic treatment of mild to moderate atopic dermatitis in non-immunocompromised adults and children 2 years of age and older, who have failed to respond adequately to other topical prescription treatments, or when those treatments are not advisable
tacrolimus (Protopic)	--	Second-line therapy for the short-term and non-continuous chronic treatment of moderate to severe atopic dermatitis in non-immunocompromised adults and children who have failed to respond adequately to other topical prescription treatments for atopic dermatitis, or when those treatments are not advisable ▪0.03% ointment approved for patients 2 years to 15 years old ▪0.03% ointment and 0.1% ointment approved for adults

Atopic Dermatitis Agents: Topical Immunosuppressives – Dosing and Availability

Drugs	Adult	Children (2 to 15 years)	Availability
crisaborole (Eucrisa)	Apply a thin layer to affected skin twice daily	Apply a thin layer to affected skin twice daily	Ointment: 60 gm tubes
dupilumab (Dupixent)	600 mg (2 x 300 mg at different injection sites) for 1 dose, followed by 300 mg every other week thereafter Administer in the thigh, abdomen (excluding area around the navel), or upper arm; rotate the injection site May be used with or without topical corticosteroids May be used with or without topical calcineurin inhibitors, but use of these should be reserved for problem areas only (e.g., face, neck, intertriginous and genital areas)	--	SC injection: 300 mg/2 mL single-dose, prefilled syringe
pimecrolimus (Elidel)	Apply a thin layer to affected skin twice daily	Apply a thin layer to affected skin twice daily	Cream: 30, 60, and 100 gm tubes
tacrolimus 0.03% (Protopic)	Apply a thin layer to affected skin twice daily	Apply a thin layer to affected skin twice daily	Ointment: 30, 60, and 100 gm tubes
tacrolimus 0.1% (Protopic)	Apply a thin layer to affected skin twice daily	--	Ointment: 30, 60, and 100 gm tubes

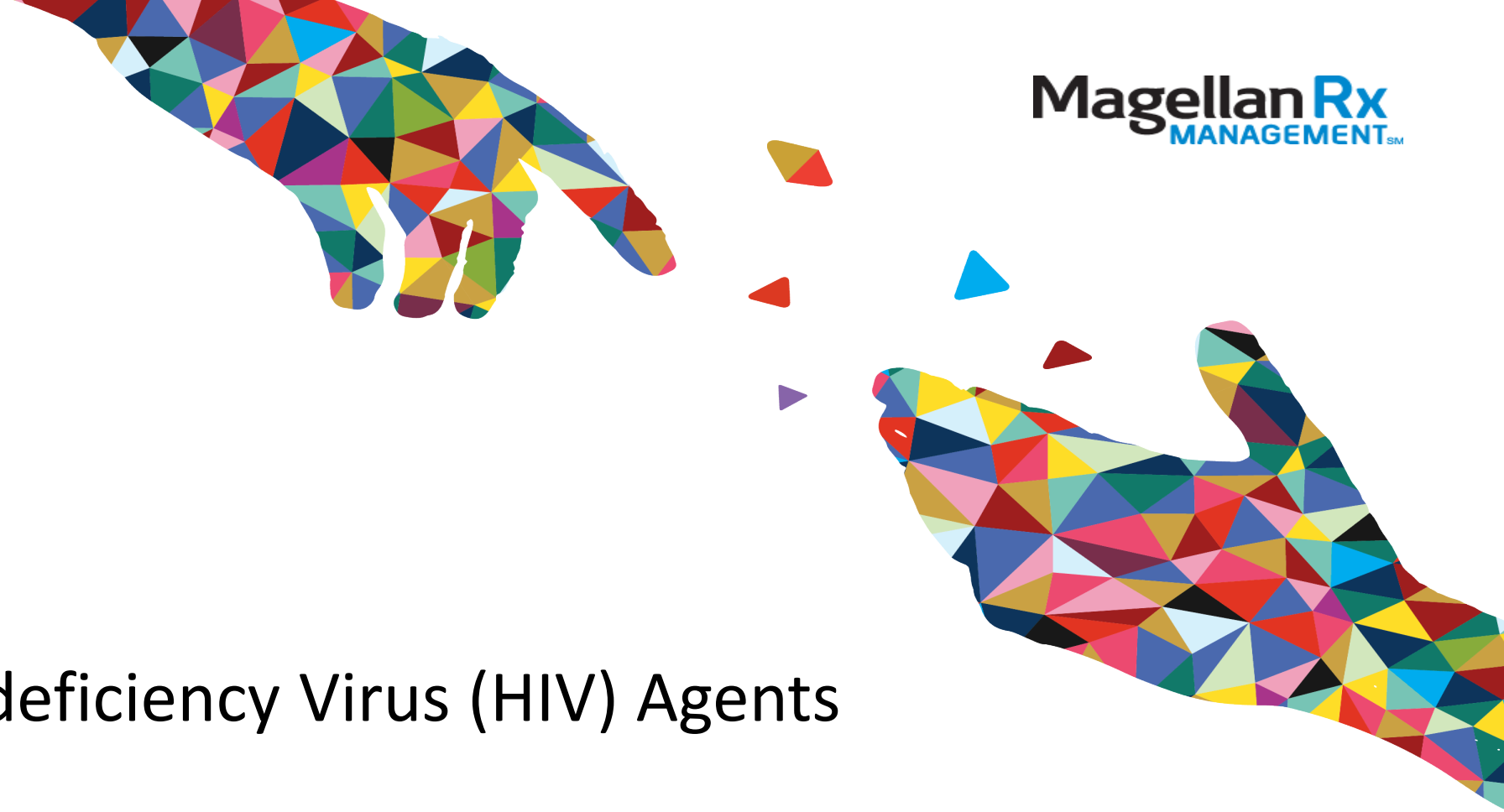
Atopic Dermatitis Agents: Dupixent

- dupilumab (Dupixent)
  - **October 2018**
    - **FDA approved a new indication for add-on maintenance treatment of moderate to severe asthma in patients ≥ 12 yo with an eosinophilic phenotype or with oral corticosteroid dependent asthma**
  - **Indication**
    - **Treatment of adult patients with moderate to severe atopic dermatitis whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable; may be used with or without topical corticosteroids**
  - **Dosage**
    - **Initial dose: 400 mg (two 200 mg injections) SC, followed by 200 mg every other week OR 600 mg (two 300 mg injections), followed by 300 mg every other week**
    - **In peds with co-morbid moderate-to-severe atopic dermatitis: Start dose at 600 mg, followed by 300 mg every other week**
    - Administer in the thigh, abdomen (excluding area around the navel), or upper arm; rotate the injection site
    - Missed doses of dupilumab (Dupixent) should be administered within 7 days of the missed dose, followed by the original schedule thereafter
  - **Availability**
    - **SC Injection: 300 mg/2 mL single-dose, prefilled syringe**
    - **A new formulation was approved as 200 mg/1.14 mL solution in a single-dose prefilled syringe with needle shield**

Guidelines - Atopic Dermatitis Agents: Topical Immunosuppressives

- **The American Academy of Dermatology (AAD), 2014**
  - State that emollients, topical corticosteroids, and topical calcineurin inhibitors are the standard of care for the treatment of AD
  - For patients whose eczema is not controlled by topical corticosteroids, or when there is a serious risk of adverse events from topical corticosteroids, topical calcineurin inhibitors should be used
  - Phototherapy is recommended as a treatment option after failure of emollients, topical steroids, and topical calcineurin inhibitors
  - Systemic immunomodulating agents are indicated for patients whose AD is not adequately controlled by topical regimens and/or phototherapy
    - Patients with this disease are prone to *Staph. aureus* infections, and treatment with oral or topical antibiotics may be useful

- **The American Academy of Allergy, Asthma, and Immunology (AAAAI) 2012**
  - Like the AAD guidelines, AAAAI guidelines state that Elidel and Protopic are reasonable treatment options for patients as second-line treatment choices
  - First-line options include hydration (emollients), moisturizers, and topical corticosteroids
    - Eucrisa and Dupixent were not available at the time of the development of these guidelines but may be considered as second-line treatment options for patients with mild to moderate atopic dermatitis
  - Although topical corticosteroids are the standard of care in the treatment of AD, dermatologic effects, such as striae, atrophy, and tachyphylaxis, as well as potential non-dermatologic effects on linear growth rate, bone density, and hypothalamic-pituitary-adrenal (HPA) axis suppression, limit the long-term use of these agents



Human Immunodeficiency Virus (HIV) Agents

Magellan Medicaid Administration

Overview of Disease State – HIV Agents

Human Immunodeficiency Virus (HIV)

- An infection that is a complex disease that results in destruction of the immune system of HIV-infected individuals
- There are 2 major subtypes of HIV:
  - HIV-1
    - The HIV-1 subtype is considered most responsible for the Acquired Immune Deficiency Syndrome (AIDS) pandemic
  - HIV-2
    - The HIV-2 subtype is thought to be less virulent and less transmissible; however, both are known to cause AIDS and are transmitted by sexual contact, through blood, and from mother-to-child
    - By far, HIV-1 is more common worldwide, and HIV-2 is more concentrated in West Africa
- The course of HIV infection varies, but the mean time from infection with HIV to the development of AIDS-related symptoms has been about 10 to 12 years in the absence of antiretroviral therapy
  - However, with the emergence of more virulent strains, time to AIDS progression may be getting shorter
  - Factors that influence the rate and severity of disease progression include age, genetic differences, and the level of virulence of the viral strain
  - Individuals infected with HIV with a specific mutation in the CCR5 gene may have a slower disease course

Overview of Disease State – HIV Agents

- First identified in 1983, but it likely entered the United States (US) in the late 1970s
- ~36.9 million people living with HIV by the end of 2017, with 21.7 million receiving antiretroviral therapy (ART) globally
  - In 2017, an estimated 47% of new infections occurred among key populations and their partners
- From 1987 through 2015, 507,351 deaths among people with AIDS in the US have been reported to the Centers for Disease Control and Prevention (CDC)
- It is estimated that only 75% of people with HIV know their status
  - Of new infections, approximately 68% are from male-to-male sexual contact, 23% from heterosexual contact, and 9% from injection drug use
- The vertical transmission rate of HIV from mother-to-child has significantly decreased in the US and abroad
  - A significant reason for the decrease in the US is associated with routine testing of pregnant women during prenatal care and the provision of antiretrovirals during pregnancy and delivery
  - Despite perinatal transmission being the primary means of childhood HIV infection, the risk can be reduced to less than 1% if recommended preventative measures are followed
- The global decline in new cases coupled with an increase in survivability of HIV/AIDS has been attributed to the increased availability of antiretroviral treatments, access to effective prevention strategies, and the improvement in care and support of those living with HIV/AIDS
  - The Joint United Nations Programme on HIV/AIDS (UNAIDS), in partnership with the World Health Organization (WHO), has updated their strategy to end the AIDS epidemic by 2030
  - According to the UNAIDS 2016 to 2021 strategy, the target of 15 million people receiving HIV treatment by 2015 was reached 9 months earlier than expected
  - Newly infected HIV patients dropped from 3.4 million to 1.8 million from 1996 to 2017, as well as a decline in the number of children acquiring HIV by 35% from 2010 to 2017

Overview of Disease State – HIV Agents

- Eight therapeutic classes represent the drug treatment options for HIV/AIDS:
    1. Nucleoside and nucleotide reverse transcriptase inhibitors (NRTIs)
    2. Non-nucleoside reverse transcriptase inhibitors (NNRTIs)
    3. Protease inhibitors (PIs)
    4. Integrase inhibitors (INSTI)
    5. CCR5 antagonist
    6. Fusion inhibitors
    7. Pharmacokinetic enhancers
    8. Monoclonal antibody (ibalizumab-uiyk; Trogarzo)

    - Initial regimen selection should be guided by patient characteristics, including comorbidities, drug-drug interaction possibilities, toxicity risk, regimen complexity, and virologic efficacy
    - Alternative regimens may be more desirable if individual patient needs warrant it
    - Alternate regimens identified by the consensus group are deemed efficacious but may have select disadvantages compared to the preferred regimens

HIV Agents – Indications

Drugs	Generic	Indications
CCR5 Antagonist		
maraviroc (Selzentry), MVC	**---**	Combination antiretroviral treatment of patients ≥ 2 years old and ≥ 10 kg infected with only CCR5-tropic HIV-1
Fusion Inhibitor		
enfuvirtide (Fuzeon), T20 or ENF	**---**	Treatment of HIV-1 infection in treatment-experienced patients with evidence of HIV-1 replication despite ongoing antiretroviral therapy in combination with other antiretrovirals
Integrase Strand Transfer Inhibitors (INSTIs)		
dolutegravir (Tivicay), DTG	**---**	In combination with other antiretroviral agents for the treatment of HIV-1 infection in adults and children ≥ 6 years of age and weighing ≥ 30 kg; In combination with rilpivirine, as a complete regimen to replace the current antiretroviral regimen in those who are virologically suppressed (HIV-1 RNA < 50 copies/mL) on a stable antiretroviral regimen for ≥ 6 months with no history of treatment failure or known substitutions associated with resistance to either antiretroviral components
raltegravir (Isentress, Isentress HD), RAL	**---**	In combination with other antiretroviral agents for the treatment of HIV-1 infection in patients weighing ≥ 2 kg

HIV Agents – Indications

Drugs	Generic	Indications
Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)		
delavirdine (Rescriptor), DLV	---	Treatment of HIV-1 infection in combination with ≥ 2 other active antiretroviral agents when therapy is warranted
doravirine (Pifeltro), DOR	---	In combination with other antiretroviral agents for the treatment of HIV-1 infection in adult patients with no prior antiretroviral treatment history
efavirenz (Sustiva), EFV	X	In combination with other antiretroviral agents for the treatment of HIV-1 infection in adults and pediatric patients ≥ 3 months of age who weigh ≥ 3.5 kg
etravirine (Intelence), ETR	---	In combination with other antiretroviral agents for the treatment of HIV-1 infection in treatment-experienced patients ≥ 2 years old
nevirapine (Viramune), NVP	X	In combination with other antiretroviral agents for the treatment of HIV-1 infection in adults and in pediatric patients ≥ 15 days old
nevirapine extended-release (Viramune XR), NVP	X	In combination with other antiretroviral agents for the treatment of HIV-1 infection in adults and in children ≥ 6 years of age with a BSA ≥ 1.17 m2
rilpivirine (Edurant), RPV	---	In combination with other antiretroviral agents for the treatment of HIV-1 infection in treatment-naïve patients ≥ 12 years of age with HIV-1 RNA ≤ 100,000 copies/mL

HIV Agents – Indications

Drugs	Generic	Indications
Nucleoside Reverse Transcriptase Inhibitors (NRTIs)		
abacavir (Ziagen), ABC	**X**	In combination with other antiretroviral agents for the treatment of HIV-1 infection
didanosine (Videx, Videx EC), ddI,	**X**	In combination with other antiretroviral agents for the treatment of HIV-1 infection
emtricitabine (Emtriva), FTC	**---**	In combination with other antiretroviral agents for the treatment of HIV-1 infection
lamivudine (Epivir), 3TC	**X**	In combination with other antiretroviral agents for the treatment of HIV-1 infection Limitation of Use: The dosage of this product is for HIV and not for hepatitis B virus (HBV)
stavudine (Zerit), d4t	**X**	In combination with other antiretroviral agents for the treatment of HIV-1 infection
zidovudine (Retrovir), AZT	**X**	In combination with other antiretroviral agents for the treatment of HIV-1 infection; Prevention of maternal-fetal HIV-1 transmission
Nucleotide Reverse Transcriptase Inhibitor (NRTI)		
tenofovir disoproxil fumarate (Viread), TDF	**X**	In combination with other antiretroviral agents for the treatment of HIV-1 infection in adults and pediatric patients ≥ 2 years of age; Treatment of chronic hepatitis B (an infection with HBV) in adults ages ≥ 18 years and pediatric patients ≥ 2 years of age weighing ≥ 10 kg
Pharmacokinetic Enhancer		
cobicistat (Tybost), COBI or c	**---**	In combination with atazanavir or darunavir to increase their systemic exposure once daily in combination with other antiretroviral agents in the treatment of HIV-1 infection

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HIV Agents – Indications

Drugs	Generic	Indications
Protease Inhibitors (PIs)		
atazanavir (Reyataz), ATV	**X**	In combination with other antiretroviral agents for the treatment of HIV-1 infection; Treatment of HIV-1 infection in pediatric patients ≥ 3 years of age who weigh ≥ 5 kg
darunavir (Prezista), DRV	**---**	Treatment of HIV-1 infection in adult patients, including pregnant women; Treatment of HIV-1 infection in pediatric patients ≥ 3 years of age who weigh ≥ 10 kg; Limitation of use: Prezista must be co-administered with ritonavir and with other antiretroviral agents
fosamprenavir (Lexiva), FPV	**X**	In combination with other antiretroviral agents for the treatment of HIV-1 infection
indinavir (Crixivan), IDV	**---**	In combination with other antiretroviral agents for the treatment of HIV-1 infection
nelfinavir (Viracept), NFV	**---**	In combination with other antiretroviral agents for the treatment of HIV-1 infection
ritonavir (Norvir), RTV or r	**X**	In combination with other antiretroviral agents for the treatment of HIV-1 infection
saquinavir (Invirase), SQV	**---**	Treatment of HIV-1 infection in combination with ritonavir and other antiretroviral agents in adults (≥ 16 years old)
tipranavir (Aptivus), TPV	**---**	Co-administered with ritonavir for combination antiretroviral treatment of HIV-1 infected patients who are treatment-experienced and infected with HIV-1 strains resistant to > 1 protease inhibitor; not indicated for use in treatment-naïve patients
Recombinant Monoclonal Antibody		
ibalizumab-uiyk (Trogarzo)	**---**	In combination with other antiretroviral(s) for the treatment of HIV-1 infection in heavily treatment-experienced adults with multidrug-resistant HIV-1 infection failing their current antiretroviral regimen

HIV Agents – Indications

Drugs	Generic	Indications
Combination Products – Nucleos(t)ide Reverse Transcriptase Inhibitors (NRTIs)		
abacavir/lamivudine (Epzicom), ABC/3TC	X	A co-formulated product containing 2 NRTIs used in combination with other antiretrovirals for the treatment of HIV-1 infection in adults and pediatric patients weighing ≥ 25 kg
abacavir/lamivudine/ zidovudine (Trizivir), ABC/3TC/AZT	X	A co-formulated product containing 3 NRTIs used in combination with other antiretrovirals or alone for the treatment of HIV-1 infection in adults and pediatric patients weighing ≥ 40 kg
emtricitabine/tenofovir alafenamide (Descovy), FTC/TAF	---	A combination product containing 2 NRTIs used in combination with other antiretroviral agents for the treatment for HIV-1 infection in adults and pediatric patients weighing ≥ 35 kg; In combination with antiviral agents (other than protease inhibitors that require CYP3A inhibitors) for HIV-1 in pediatric patients weighing ≥ 25 kg to < 35 kg Limitation of Use: it is not indicated for use as pre-exposure prophylaxis (PrEP) to reduce the risk of sexually acquired HIV-1 in high-risk adults
lamivudine/tenofovir disoproxil fumarate (Cimduo), 3TC/TDF	---	A combination of 2 nucleos(t)ide reverse transcriptase inhibitors indicated in combination with other antiretroviral agents for the treatment of HIV-1 infection in adult and pediatric patients weighing ≥ 35 kg
lamivudine/zidovudine (Combivir), 3TC/AZT	X	A co-formulated product containing 2 NRTIs used in combination with other antiretroviral agents for the treatment of HIV-1 infection in adults and pediatric patients weighing ≥ 30 kg
tenofovir disoproxil fumarate/emtricitabine (Truvada), TDF/FTC	---	A co-formulated product containing 2 NRTIs used in combination with other antiretroviral agents for the treatment of HIV-1 infection in adults and pediatric patients weighing ≥ 17 kg; Indicated in combination with safer sex practices for pre-exposure prophylaxis (PrEP) to reduce the risk of sexually acquired HIV-1 in adults at high risk and adolescents weighing ≥ 35 kg

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HIV Agents – Indications

Drugs	Generic	Indications
Combination Products – Protease Inhibitors (PIs) or PIs + Pharmacokinetic Enhancer		
atazanavir/cobicistat (Evotaz), ATV/c	---	A co-formulated product containing a PI and a pharmacokinetic enhancer used in combination with other antiretroviral agents for the treatment of HIV-1 infection in adults
darunavir/cobicistat (Prezcobix), DRV/c	---	A co-formulated product containing a PI and a pharmacokinetic enhancer used in combination with other antiretroviral agents for the treatment of HIV-1 infection in treatment-naïve and treatment-experienced adults with no darunavir resistance-associated substitutions (V11I, V32I, L33F, I47V, I50V, I54L, I54M, T74P, L76V, I84V, L89V)
lopinavir/ritonavir (Kaletra), LPV/r	**X**	A co-formulated product containing 2 PIs used in combination with other antiretroviral agents for the treatment of HIV-1 infection in adults and pediatric patients (≥ 14 days old)
Combination Products – Multiple Classes		
bictegravir/emtricitabine/ tenofovir alafenamide (Biktarvy), BIC/FTC/TAF	---	A co-formulated product containing an INSTI and 2 NRTIs approved as a complete regimen for the treatment of HIV-1 infection in adults who are antiretroviral-naive or who are virologically suppressed (HIV-1 RNA < 50 copies/mL) on their current, stable antiretroviral regimen for ≥ 3 months with no history of treatment failure and no known substitutions associated with resistance to its individual components
darunavir/cobicistat/ emtricitabine/tenofovir alafenamide (Symtuza), DRV/c/FTC/TAF	---	A co-formulated product containing a PI, a CYP3A inhibitor, and 2 NRTIs indicated in adults who are either antiretroviral-naive or virologically suppressed (HIV-1 RNA < 50 copies/mL) while on stable antiretroviral therapy for ≥ 6 months and have no known substitutions associated with resistance to darunavir or tenofovir
dolutegravir/abacavir/ lamivudine (Triumeq), DTG/ABC/3TC	---	A co-formulated product containing 1 INSTI and 2 NRTIs indicated for the treatment of HIV-1 infection in adults and pediatric patients weighing ≥ 40 kg
dolutegravir/rilpivirine (Juluca), DTG/RPV	---	A co-formulated product containing an INSTI and a NNRTI indicated as a complete regimen for the treatment of HIV-1 infection in adults to replace the current antiretroviral regimen in those who are virologically suppressed (HIV-1 RNA < 50 copies/mL) on a stable antiretroviral regimen for ≥ 6 months with no history of treatment failure and no known substitutions associated with resistance to its individual components

HIV Agents – Indications

Drugs	Generic	Indications
Combination Products – Multiple Classes (Continued)		
doravirine/lamivudine/ tenofovir disoproxil fumarate (Delstrigo), DOR/3TC/TDF	**---**	A co-formulated product containing NNRTI and 2 NRTIs indicated as a complete regimen for the treatment of HIV-1 infection in adult patients with no antiretroviral treatment history
efavirenz/lamivudine/ tenofovir disoproxil fumarate (Symfi), EFV/3TC/TDF	**---**	A co-formulated product containing 1 NNRTI and 2 NRTIs indicated as a complete regimen for the treatment of HIV-1 infection in adult and pediatric patients weighing ≥ 40 kg
efavirenz/lamivudine/ tenofovir disoproxil fumarate (Symfi Lo), EFV/3TC/TDF	**---**	A co-formulated product containing 1 NNRTI and 2 NRTIs indicated as a complete regimen for the treatment of HIV-1 infection in adult and pediatric patients weighing ≥ 35 kg
elvitegravir/cobicistat/ emtricitabine/tenofovir alafenamide (TAF) (Genvoya), EVG/c/FTC/TAF	**---**	A co-formulated product containing 1 INSTI, 1 pharmacokinetic enhancer, and 2 NRTIs for the treatment of HIV-1 infection in adults and pediatric patients weighing ≥ 25 kg who have no antiretroviral treatment history or to replace the current antiretroviral regimen in those who are virologically-suppressed (HIV-1 RNA < 50 copies/mL) on a stable antiretroviral regimen for ≥ 6 months with no history of treatment failure and no known substitutions associated with resistance to its components
elvitegravir/cobicistat/ emtricitabine/tenofovir disoproxil fumarate (Stribild), EVG/c/FTC/TDF	**---**	A co-formulated product containing 1 INSTI, 1 pharmacokinetic enhancer, and 2 NRTIs as a complete regimen for the treatment of HIV-1 infection in adults and pediatric patients ≥ 12 years old and weighing ≥ 35 kg who are antiretroviral treatment-naïve or to replace the current antiretroviral regimen in those who are virologically-suppressed (HIV-1 RNA < 50 copies/mL) on a stable antiretroviral regimen for ≥ 6 months with no history of treatment failure and no known substitutions associated with resistance to the individual components
emtricitabine/rilpivirine/ tenofovir alafenamide (Odefsey), FTC/RPV/TAF	**---**	A combination product containing 2 NRTIs and 1 NNRTI indicated for the treatment of HIV-1 infection in patients ≥ 12 years of age as initial therapy in treatment-naïve patients with HIV-1 RNA ≤ 100,000 copies/mL or to replace a stable antiretroviral regimen in those who are virologically-suppressed (HIV-1 RNA < 50 copies/mL) for ≥ 6 months with no history of treatment failure and no known substitutions associated with resistance to the individual components
rilpivirine/emtricitabine/ tenofovir disoproxil fumarate (Complera), RPV/FTC/TDF	**---**	A co-formulated product containing 2 NRTIs and 1 NNRTI used as a complete regimen for the treatment of HIV-1 infection in treatment-naïve patients ≥ 12 years old and weighing ≥ 35 kg with HIV-1 RNA ≤ 100,000 copies/mL at the start of therapy; As an alternate regimen for the treatment of HIV-1 infection in certain adult patients who are virologically suppressed (HIV-1 RNA < 50 copies/mL) on a stable ritonavir-boosted PI regimen at start of therapy in order to replace their current antiretroviral treatment regimen
tenofovir disoproxil fumarate/emtricitabine/ efavirenz (Atripla), TDF/FTC/EFV	**---**	A co-formulated product containing 2 NRTIs and 1 NNRTI used alone as a complete regimen or in combination with other antiretroviral agents for the treatment of HIV-1 infection in adults and pediatric patients weighing ≥ 40 kg

HIV Agents - Dosing/Availability

- See HIV Agents Appendix

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HIV Agents – Guidelines

- **Department of Health and Human Services (DHHS) Guidelines, 2018**
  - The updated October 2018 Department of Health and Human Services (DHHS) Guidelines for the Use of Antiretrovirals in HIV-1 Infected Adults and Adolescents continue to recommend to initiate ART in patients with acute and recent HIV-1 infection regardless of CD4 cell count under the evidence rating of A1
  - The recommendations were strongly based on findings from 2 large studies, START and TEMPRANO, that demonstrated a 50% reduction in morbidity and mortality among HIV-infected patients with CD4 cell count > 500 cells/mm^3
    - Although these studies did not include adolescents, the recommendation to initiate ART therapy early has been extended to this population
  - Antiretroviral therapy (ART) is recommended for all persons with HIV to prevent transmission and reduce the morbidity and mortality, regardless of CD4 T lymphocyte cell count
    - In select patients, ART may be deferred due to clinical and/or psychosocial factors; however, ART should be initiated as soon as possible
  - Patients who are considering ART should be well informed of the risks and benefits of both treatment and postponing treatment, in order to make an informed decision
    - Possible therapeutic complications from non-adherence or adverse reactions need to be considered by the patient to ensure commitment to the treatment once initiated
    - The only individuals who are generally not recommended for ART are those unwilling or unable to commit to the treatment

- **International AIDS Society (IAS), 2018**
  - Recommendations for HIV Drug Resistance states that although ART has diminished HIV treatment failure rates, overall transmission of drug-resistant viruses has not diminished
  - Therefore, IAS continues to recommend testing for HIV drug resistance in drug-naïve individuals and in patients in whom ART is failing as this can play a pivotal role in preventing and managing ART resistance

HIV Agents – Guidelines

- **Department of Health and Human Services (DHHS) Guidelines, 2018**
  - Recommend that CD4 counts be measured every 3 to 6 months during the first 2 years of therapy, if viremia develops while patient is on antiretroviral therapy, if ART initiation is delayed, if there are ART modifications, and if CD4 count reaches < 300 cells/mm^3
    - Testing is then recommended to be every 12 months after 2 years on antiretroviral therapy with a consistently suppressed viral load
  - Drug-resistance testing is recommended at entry into care regardless of whether therapy will be initiated immediately or deferred
    - They also recommend mutation testing for reverse transcriptase (RT), protease (PR) genes, and INSTIs if needed
    - If therapy is deferred, repeat testing should be considered at time of therapy initiation
    - Resistance testing is also recommended in the setting of virologic failure while the patient is taking the drug or within 4 weeks after discontinuing therapy
    - If more than 4 weeks have lapsed since discontinuation, resistance testing may still provide useful information to guide therapy
  - Genotypic testing, as described above, should be employed to detect resistance
    - In patients who are experiencing treatment failure and for whom conventional HIV RNA genotypic drug-resistance testing is unavailable or unsuccessful, next generation sequencing genotypic resistance assay that analyzes pro-viral DNA can be considered
    - However, it is imperative to interpret the results with caution as these assays can miss some or all previously existing drug-resistance mutations
    - When such testing is obtained, results should be combined with all prior genotypic and phenotypic test results to construct a cumulative genotype, which will incorporate all current and previously detected drug-resistance mutations
    - It is important to note that the usefulness of these assays in a clinical setting is still under investigation and has yet to be fully determined
  - A pro-viral DNA tropism assay can be utilized for patients with undetectable HIV-1 RNA when a CCR5 antagonist (e.g., maraviroc) is considered for use in a new regimen, such as part of a regimen switch or simplification
    - The guidelines recommend that, for treatment-experienced patients with multi-drug resistant HIV, the clinician should consider enrolling the patient in a clinical trial of investigational drugs or contacting pharmaceutical sponsors that may have investigational agents available
  - Hemoglobin A1C, HIV serology, and hepatitis C serology testing are also recommended
  - Notably, patients should be screened for both hepatitis B or C virus at entry into care as having the co-infection may impact the initiation of ART

HIV Agents – Guidelines

- **International AIDS Society (IAS), 2018**
  - They state that HIV testing is recommended at least once for anyone who has ever been sexually active and more often for individuals at ongoing risk for infection
  - The panel continues to conclude that, after confirmed diagnosis of HIV infection, antiretroviral therapy should be started as soon as possible, including immediately after diagnosis, regardless of CD4 cell count
  - Samples for HIV-1 RNA level, CD4 cell count, HIV genotype for NRTI, NNRTI and PI, laboratory tests to exclude active viral hepatitis, and chemistries should be drawn before beginning ART, but treatment may be started before results are available
  - Results of testing for HLA-B*5701 allele should be available if an abacavir-containing regimen is anticipated
  - Regimens should be selected or changed based on resistance test results with consideration of dosing frequency, pill burden, adverse effect profiles, co-morbidities, and drug interactions
  - Patients receiving antiretroviral treatment should be monitored regularly and treatment failure should be detected and managed early, with the goal of therapy, even in previously treated patients, being HIV-1 RNA suppression below commercially available assay quantification limits
  - Furthermore, they indicate that an INSTI plus 2 NRTIs is generally recommended for initial therapy, with unique patient circumstances (e.g., concomitant diseases and conditions, potential for pregnancy, cost) guiding the treatment choice
  - NNRTIs and abacavir should not be used for rapid ART start
  - The group states that TDF is not recommended for individuals with or at risk for kidney or bone disease (osteopenia or osteoporosis); however, if it is not available or if there is a substantial cost difference, TDF (with emtricitabine or lamivudine) is effective and generally well tolerated
  - CD4 cell count, HIV RNA level, genotype, and other laboratory tests for general health and co-infections are recommended at specified points before and during ART
  - If a regimen switch is indicated, treatment history, tolerability, adherence, and drug resistance history should first be assessed: 2 or 3 active drugs are recommended for a new regimen

HIV Agents – Guidelines

- **International AIDS Society (IAS), 2018**

Initial Antiretroviral Treatment of Adults (IAS) All Recommendations Have Rating of A1a Rating of Recommendations: A = Strong Rating of Evidence: Ia= Evidence from ≥ 1 randomized controlled trial published in peer-reviewed literature		
INSTI plus 2 NRTIs	**NNRTI plus 2 NRTIs**	**Ritonavir-boosted protease inhibitor plus 2 NRTIs**
bictegravir + tenofovir alafenamide (TAF) + emtricitabine	efavirenz + TDF + emtricitabine	darunavir + cobicistat + TAF (or TDF) + emtricitabine
dolutegravir + abacavir + lamivudine	rilpivirine + TAF (or TDF) + emtricitabine (if pretreatment HIV RNA level is < 100,000 copies/mL and CD4 cell count is > 200/µL)	darunavir + ritonavir + TAF (or TDF) + emtricitabine
dolutegravir + TAF + emtricitabine		
elvitegravir + cobicistat + TAF (or tenofovir disoproxil fumarate [TDF]) + emtricitabine		
raltegravir + TAF (or TDF) + emtricitabine		

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HIV Agents – Guidelines

- **<u>Department of Health and Human Services (DHHS) Guidelines, 2018</u>**
  - Recommendations to consider before initiating dolutegravir (DTG) and other integrase strand inhibitors as initial therapy
    - Pregnancy testing should be performed in those of childbearing potential prior to initiation of ART due to preliminary data showing an increased risk of neural tube defects (NTDs) in infants born to women who were receiving DTG at time of conception
    - Dolutegravir should not be prescribed for the following individuals: those who are pregnant and within 12 weeks post-conception; patients of childbearing potential who are planning to become pregnant; and those who are of childbearing potential, are sexually active, and are not using effective contraception
      - For those who are using effective contraception, a DTG-based regimen can be considered after weighing the risks and benefits. However, it is not known if other INSTIs pose a similar risk of NTDs
      - In addition, in patients who are pregnant, bictegravir is not recommended due to insufficient safety data, and elvitegravir/cobicistat is not recommended due to reportedly low elvitegravir plasma concentrations during the second and third trimesters
      - There is limited raltegravir data during the first trimester in the US. Currently, it is not known whether the link between DTG and NTDs represents a class effect; however, this potential risk should be discussed with patients of childbearing potential who prefer an INSTI-containing regimen

HIV Agents – Guidelines

- **Department of Health and Human Services (DHHS) Guidelines, 2018**

Treatment Options for Most Treatment-Naïve Adults and Adolescents (DHSS)	
INSTI-Based Regimen	**Co-formulated Availability**
bictegravir + tenofovir alafenamide (TAF) + emtricitabine (AI)	ABC/3TC FTC/TAF 3TC/TDF TDF/FTC BIC/TAF/FTC DTG/ABC/3TC EVG/c/TDF/FTC EVG/c/TAF/FTC
dolutegravir + abacavir + lamivudinea – only for patients who are HLA-B* 5701 negative (AI)	
dolutegravir + tenofovirb + emtricitabinea (AI)	
raltegravir + TDF + emtricitabinea (BI)	
raltegravir + TAF + emtricitabinea (BII)	

Alternative/Other Treatment Options in Treatment-Naïve Adults and Adolescents (DHSS) – Recommended for Certain Clinical Situations			
INSTI-Based	**NNRTI-Based**	**Protease Inhibitor-Based**	**Co-formulated Availability**
elvitegravir + cobicistat + tenofovirb + emtricitabinea (BI)	doravirine + tenofovir alafenamideb + lamivudine (BIII)	atazanavir + cobicistat (or ritonavir) + tenofovirb + emtricitabine (BI)	ATV/c DRV/c LPV/r ABC/3TC FTC/TAF 3TC/TDF TDF/FTC DOR/TDF/3TC DRV/c/FTC/TAF EFV 600 mg/ TDF/3TC EFV/3TC/TDF FTC/RPV/TAF RPV/FTC/TDF TDF/FTC/EFV
	doravirine + tenofovir disoproxil fumarateb + lamivudine (BI)		
	efavirenz + lamivudine+ TDF (BI)		
	efavirenz + emtricitabine + TDF (BI)		
	efavirenz + emtricitabine + TAF (BII)		
raltegravir + abacavir + lamivudinea – only for patients who are HLA-B NA < 100,000 copies/mL (CII)	rilpivirine + tenofovirb + emtricitabinea – only for patients with HIV RNA < 100,000 copies/mL and CD4 > 200 cells/mm3 (BI)	darunavir + ritonavir + tenofovirb + emtricitabinea (AI)	
		darunavir + cobicistat + tenofovirb + emtricitabinea (AI)	
		darunavir + cobicistat (or ritonavir) + abacavir + lamivudinea (BII) — only for patients who are HLA-B*5701 negative	
		darunavir + ritonavir + lamivudine once daily (CI), if ABC, TAF, and TDF cannot be used	
		darunavir + ritonavir + raltegravir twice daily (CI) if HIV RNA < 100,000 copies/mL, CD4 > 200 cells/mm3, and if ABC, TAF, and TDF cannot be used	
		dolutegravir + lamivudine (BI), if ABC, TAF, and TDF cannot be used	

HIV Agents – Guidelines

- **Department of Health and Human Services (DHHS) Guidelines, 2018**
  - **Pediatric Recommendations**

Preferred Regimens for Treatment-Naïve Children and Adolescents	
Infants, Birth to Age < 14 days	2 NRTIs plus nevirapine
	2 NRTIs plus raltegravir
Children ≥ 14 days postnatal and < 3 years	2 NRTIs plus lopinavir/ritonavir (must be ≥ 42 weeks postmenstrual age)
	2 NRTIs plus raltegravir
Children ≥ 3 years to < 6 years	2 NRTIs plus atazanavir/ritonavir
	2 NRTIs plus darunavir/ritonavir (twice-daily)
	2 NRTIs plus raltegravir
Children ≥ 6 years to < 12 years	2 NRTIs plus atazanavir/ritonavir
	2 NRTIs plus dolutegravir (only for children and adolescents weighing ≥ 30 kg)
Adolescents ≥ 12 years (sexual maturity rating 1 to 3*; see adult guidelines for those with higher sexual maturity ratings)	2 NRTIs plus atazanavir/ritonavir
	2 NRTIs plus dolutegravir (only for children and adolescents weighing ≥ 30 kg)
	2 NRTIs plus darunavir/ritonavir (once daily)
	2 NRTIs plus elvitegravir/cobicistat (for children and adolescents weighing ≥ 35 kg)

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HIV Agents – Guidelines

- **Department of Health and Human Services (DHHS) Guidelines, 2018**
  - **Pediatric Recommendations**

Alternative Regimens for Treatment-Naïve Children and Adolescents	
Children ≥ 14 days to < 3 years	2 NRTIs plus NVP (should not be used in postpubertal girls with CD4 count greater than 250/mm3)
Children ≥ 3 months to < 3 years and weighing ≥ 10 kg	2 NRTIs plus atazanavir/ritonavir
Children ≥ 3 years to < 6 years	2 NRTIs plus efavirenz (not recommended as initial therapy in children aged ≥ 3 months to 3 years)
	2 NRTIs plus lopinavir/ritonavir
Children ≥ 6 years to < 12 years	2 NRTIs plus darunavir/ritonavir (twice daily)
	2 NRTIs plus efavirenz (with reliable contraception if applicable)
	2 NRTIs plus elvitegravir/cobicistat
	2 NRTIs plus lopinavir/ritonavir
	2 NRTIs plus raltegravir
Children ≥ 12 years	2 NRTIs plus efavirenz (with reliable contraception if applicable)
	2 NRTIs plus raltegravir
	2 NRTIs plus rilpivirine

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HIV Agents – Guidelines

- **Department of Health and Human Services (DHHS) Guidelines, 2018**
  - **Pediatric Recommendations**

Preferred 2-NRTI Backbone Treatment-Naïve Children and Adolescents	
Children, birth to < 3 months	ZDV plus (3TC or FTC)
Children ≥ 3 months to < 6 years	ABC plus (3TC or FTC)
	ZDV plus (3TC or FTC)
Children ≥ 6 years (sexual maturity rating 1 to 3; see adult guidelines for those with higher sexual maturity ratings)	ABC plus (3TC or FTC)
	FTC/TAF (FTC/TAF is FDA-approved for children weighing ≥ 25 kg when used in the single-tablet regimen EVG/COBI/FTC/TAF or as FTC/TAF in combination with an NNRTI or INSTI. There is insufficient data to recommend use of FTC/TAF in combination with a boosted PI in children weighing < 35 kg. For children and adolescents weighing ≥ 35 kg, TAF can be used in the single-tablet regimen EVG/COBI/FTC/TAF, or as FTC/TAF in combination with an NNRTI, an INSTI, or a boosted PI)

Alternative 2-NRTI Backbone for Treatment-Naïve Children and Adolescents	
Children ≥ 3 months	ZDV plus ABC
Children ≥ 2 years to 12 years	TDF plus (3TC or FTC)
Children ≥ 6 years (sexual maturity rating 1 to 3)	ZDV plus (3TC or FTC)

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HIV Agents – Guidelines

- **Department of Health and Human Services (DHHS) Guidelines, 2018**
  - **Pregnancy Recommendations**

Initial Combination Regimens for Antiretroviral-Naïve Pregnant Women		
2 NRTI Backbone Options	**Protease Inhibitor-Based Regimen**	**INSTI-Based Regimen**
abacavir/lamivudine (should not be used in patients who test positive for HLA-B*5701)	atazanavir/ritonavir + a preferred 2-NRTI backbone regimen (not recommended if pretreatment HIV RNA is > 100,000 copies/mL.)	raltegravir + a preferred 2-NRTI backbone regimen (twice daily dosing)
tenofovir disoproxil fumarate/ emtricitabine tenofovir disoproxil fumarate/ lamivudine	darunavir/ritonavir + a preferred 2-NRTI backbone regimen	dolutegravir + abacavir + emtricitabine dolutegravir + a preferred 2-NRTI backbone regimen (after the first trimester) NOTE: dolutegravir is not recommended for use in pregnant women during first trimester

Alternative Initial Combination Regimens for Antiretroviral-Naïve Pregnant Women		
2 NRTI Backbone Options	**Protease Inhibitor-Based Regimen**	**INSTI-Based Regimen**
zidovudine/ lamivudine	lopinavir/ritonavir + a preferred 2-NRTI backbone regimen (twice daily) NOTE: Dose increase recommended in 3rd trimester	efavirenz/ tenofovir disoproxil fumarate/ emtricitabine or efavirenz/ tenofovir disoproxil fumarate/ lamivudine or efavirenz + a preferred 2-NRTI backbone regimen NOTE: Antenatal and postpartum depression screening is recommended. Caution remains due to birth defects seen in primate studies.
		rilpivirine/tenofovir disoproxil fumarate/ emtricitabine or rilpivirine + a preferred 2-NRTIbackbone regimen

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HIV Agents – Guidelines

- **Pre-exposure Prophylaxis (PrEP)**
  - Daily oral PrEP has been shown to be safe and effective in reducing the risk of sexual HIV acquisition in adults. Therefore:
    - PrEP is recommended as 1 prevention option for sexually-active men who have sex with men (MSM) at substantial risk of HIV acquisition (IA)
    - PrEP is recommended as 1 prevention option for adult heterosexually active men and women who are at substantial risk of HIV acquisition (IA)
    - PrEP is recommended as 1 prevention option for adult persons who inject drugs (PWID) at substantial risk of HIV acquisition (IA)
    - PrEP should be discussed with heterosexually-active women and men whose partners are known to have HIV infection (e.g., HIV-discordant couples as one of several options to protect the uninfected partner during conception and pregnancy (IIB)
  - Before prophylaxis is initiated, clinicians should determine eligibility for PrEP by ensuring the individual is HIV-negative, at high risk for acquiring the infection, and has a calculated creatinine clearance (via Cockcroft-Gault) ≥ 60 mL/min
  - It is advisable to evaluate sexual partner therapy status, pregnancy/lactation status, acute HIV infection symptoms, and screen for comorbid conditions (HBV, sexually transmitted infections [STIs])
  - Conduct STI testing in sexually active persons with signs or symptoms of infection and in asymptomatic MSM at high risk for recurrent bacterial STIs (e.g., those with syphilis, gonorrhea, or chlamydia at prior visits or multiple sex partners)
    - Updated CDC guidelines state that for gonorrhea and chlamydia testing in MSM, pharyngeal, rectal, and urine specimens should be collected (“3-site testing”) to maximize the identification of infection, which may occur at any of these sites of exposure during sex
  - No more than 90 days of PrEP should be prescribed initially; subsequent dosing relies on follow-up HIV tests being negative since there is a high risk of antiretroviral resistance developing if the regimen is used while HIV infected. Non-adherence to the regimen is a criterion for discontinuation
    - It is critical that education be provided to the user on both pharmacologic and non-pharmacologic means to minimize the risk of HIV transmission
    - Individuals who become infected should discontinue PrEP and be offered a preferred antiretroviral treatment regimen
  - Transgender persons are those whose sex at birth differs from their self-identified gender
    - Although the effectiveness of PrEP for transgender women has not yet been definitively proven in trials, and trials have not been conducted among transgender men
    - PrEP has been shown to reduce the risk for HIV acquisition during anal sex and penile-vaginal sex; therefore, its use may be considered in all persons at risk of acquiring HIV sexually

Asthma and COPD Agents: COPD Agents

Magellan Medicaid Administration

Overview of Disease State – COPD Agents

- Chronic obstructive pulmonary disease (COPD) is a disease state characterized by the presence of airflow obstruction due to chronic bronchitis or emphysema
  - The airflow obstruction is generally progressive, may be accompanied by airway hyperreactivity, and may be partially reversible
  - This progressive persistent obstruction or limitation of airflow is associated with an enhanced chronic inflammatory response in both the airways and the lung to noxious particles or gases
- Although the precise distinctions between chronic bronchitis and emphysema are a subject of debate, common belief holds that chronic bronchitis is responsible for 85% of COPD
  - Patients with chronic bronchitis experience intermittent airway inflammation and excessive mucus production that leads to frequent, prolonged episodes of productive cough
  - In contrast, 15% of patients with COPD suffer primarily from emphysema, in which destruction of the infrastructure of alveoli and distal airspaces that provide gas exchange and elastic recoil occurs
  - Both chronic bronchitis and emphysema predispose patients to a common collection of symptoms and impairments in respiratory function, such as reductions in forced expiratory volume in 1 second (FEV_1), forced vital capacity (FVC), FEV_1/FVC ratio, and forced expiratory flow ($FEF_{25-75\%}$)
- Exacerbations and comorbidities contribute to the overall severity in individual patients. COPD continues to be a leading cause of chronic morbidity and mortality worldwide carrying with it significant economic and social burden
  - COPD is projected by the World Health Organization (WHO) to become the third leading cause of death by 2030
  - In their 2017 National Health Interview Survey, the CDC reported that the percentage of adults who were diagnosed with chronic bronchitis in the past year was 3.5% and those that have ever been diagnosed with emphysema was 1.4%
  - However, the United States Preventive Services Task Force (USPSTF) recommends against routine screening in asymptomatic adults

Global Initiative for Chronic Obstructive Lung Disease (GOLD), 2018
World Health Organization, 2008
Centers for Disease Control and Prevention (CDC), 2016

COPD Agents – Indications

Drugs	Generic	Indications
Antimuscarinics – Short-Acting		
ipratropium inhalation solution	**X**	For maintenance treatment of bronchospasm associated with COPD, including chronic bronchitis and emphysema
ipratropium inhalation aerosol MDI (Atrovent HFA)	**---**	As a bronchodilator for maintenance treatment of bronchospasm associated with COPD, including chronic bronchitis and emphysema
Antimuscarinics – Long-Acting		
aclidinium bromide (Tudorza Pressair)	**---**	For the long-term, maintenance treatment of bronchospasm associated with chronic obstructive pulmonary disease (COPD), including chronic bronchitis and emphysema
glycopyrrolate (Lonhala Magnair)	**---**	For the long-term, maintenance treatment of airflow obstruction in patients with COPD
Glycopyrrolate (Seebri Neohaler)	**---**	For the long-term, maintenance treatment of airflow obstruction in patients with COPD
revefenacin (Yupelri)	**---**	For the long-term, maintenance treatment of airflow obstruction in patients with COPD
tiotropium inhalation powder DPI (Spiriva HandiHaler)	**---**	For the long-term, once-daily maintenance treatment of bronchospasm associated with COPD, including chronic bronchitis and emphysema To reduce COPD exacerbations
tiotropium bromide inhalation spray (Spiriva Respimat)	**---**	For the long-term, once-daily, maintenance treatment of bronchospasm associated with COPD and for reducing COPD exacerbations For the long-term, once-daily, maintenance treatment of asthma in patients ≥ 6 years old
umeclidinium (Incruse Ellipta)	**---**	For the long-term, once-daily, maintenance treatment of airflow obstruction in COPD patients
Beta$_2$-Agonist/Antimuscarinic Combinations – Short-Acting		
albuterol/ipratropium inhalation solution	**X**	For the treatment of bronchospasm associated with COPD in patients requiring more than 1 bronchodilator
albuterol/ipratropium MDI CFC-free (Combivent Respimat)	**---**	For use in patients with COPD on a regular aerosol bronchodilator who continue to have evidence of bronchospasm and require a second bronchodilator

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COPD Agents – Indications

Drugs	Generic	Indications
Beta$_2$-Agonist/Antimuscarinic Combinations – Long-Acting		
formoterol/glycopyrrolate (Bevespi Aerosphere)	---	For the maintenance treatment of airflow obstruction in patients with COPD
indacaterol/glycopyrrolate (Utibron Neohaler)	---	For the long-term, maintenance treatment of airflow obstruction in patients with COPD
tiotropium/olodaterol (Stiolto Respimat)	---	For treatment of airflow obstruction in patients with COPD
umeclidinium/vilanterol (Anoro Ellipta)	---	For the long-term, once-daily maintenance treatment of airflow obstruction in patients with COPD, including chronic bronchitis and/or emphysema
Phosphodiesterate 4 (PDE4) Inhibitor		
roflumilast (Daliresp)	---	As a treatment to reduce the risk of COPD exacerbations in patients with severe COPD associated with chronic bronchitis and a history of exacerbations

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COPD Agents – Dosing and Availability

Drugs	Adult Dose	Availability
Antimuscarinics – Short-Acting		
ipratropium bromide inhalation solution (Atrovent)	2.5 mL 3 to 4 times daily	500 mcg per 2.5 mL (0.02%)
ipratropium inhalation aerosol MDI (Atrovent HFA)	2 inhalations 4 times daily (do not exceed 12 inhalations in 24 hours)	17 mcg per actuation; 200 inhalations per package
Antimuscarinics – Long-Acting		
aclidinium bromide inhalation powder DPI (Tudorza Pressair)	1 inhalation twice daily	400 mcg per actuation; 30 and 60 actuations/package Breath activated device
glycopyrrolate inhalation solution (Lonhala Magnair)	1 mL twice daily	25 mcg per 1 mL starter kit containing 60 unit-dose vials and 1 Magnair nebulizer or refill kit containing 60 unit-dose vials and a Magnair handset refill
glycopyrrolate inhalation powder DPI (Seebri Neohaler)	1 inhalation twice daily	15.6 mcg per capsule; 60 capsules/package Breath activated device
revefenacin inhalation solution (Yupelri)	3 mL once daily via nebulizer	175 mcg per 3 mL unit-dose vial
tiotropium inhalation powder DPI (Spiriva HandiHaler)	1 inhalation daily (do not swallow capsules)	18 mcg per capsule; 30 or 90 capsules/package Breath activated device
tiotropium inhalation spray ISI (Spiriva Respimat)	COPD: 2 inhalations of 2.5 mcg/actuation once daily Asthma (adults and children ≥ 6 years old): 2 inhalations of 1.25 mcg/ actuation once daily (maximum benefits may take up to 4 to 8 weeks)	1.25, 2.5 mcg tiotropium per actuation; 60 actuations per package
umeclidinium inhalation powder DPI (Incruse Ellipta)	1 inhalation once daily	62.5 mcg per actuation; 30 actuations/package Breath activated device

COPD Agents – Dosing and Availability

Drugs	Adult Dose	Availability
Beta2-Agonist/Antimuscarinic Combination – Short-Acting		
albuterol sulfate /ipratropium bromide inhalation solution	3 mL 4 times daily (up to 2 additional 3 mL doses per day)	3 mg/0.5 mg per 3 mL
albuterol/ipratropium bromide MDI CFC-free (Combivent Respimat)	1 inhalation (spray) 4 times daily (do not exceed 6 inhalations in 24 hours)	100/20 mcg per actuation; 120 actuations/package
Beta2-Agonist/Antimuscarinic Combination – Long-Acting		
formoterol/glycopyrrolate inhalation aerosol MDI (Bevespi Aerosphere)	2 inhalations twice daily	4.8/9 mcg per actuation; 120 actuations/canister
indacaterol/glycopyrrolate inhalation powder DPI (Utibron Neohaler)	1 inhalation twice daily	27.5/15.6 mcg per capsule; 60 capsules/package Breath activated device
tiotropium/olodaterol inhalation spray ISI (Stiolto Respimat)	2 inhalations once daily	2.5/2.5 mcg per actuation; 60 actuations/package
umeclidinium/vilanterol inhalation powder DPI (Anoro Ellipta)	1 inhalation daily (administered at the same time every day)	62.5 mg umeclidinium and 25 mcg vilanterol capsules; 30 capsules each of umeclidinium and vilanterol per package (1 capsule of each provides 1 dose) Breath activated device
Phosphodiesterase 4 (PDE4) Inhibitors		
roflumilast (Daliresp)	1 tablet (500 micrograms) daily, with or without food May initiate with 250 mcg once daily for 4 weeks, then increase to 500 mcg once daily thereafter, to reduce the rate of treatment discontinuation in some patients; 250 mcg is not an effective therapeutic dose	Oral tablets: 250 mcg, 500 mcg

COPD Agents – Guidelines

- Global Initiative for Chronic Obstructive Lung Disease (GOLD), 2019
  - Stresses that a diagnosis of COPD should be considered in any individual who has dyspnea, chronic cough/sputum production, and a history of exposure to risk factors specific to the disease
  - Spirometry is required to effectively establish a clinical diagnosis of COPD
  - The COPD Assessment Test (CAT, 0 to 40) or the Clinical COPD Questionnaire (CCQ) is recommended for a comprehensive assessment of symptoms. The Modified British Medical Research Council questionnaire may be used, but only assesses breathlessness
  - Prior to 2017, patient groups were categorized into an alphabetic (ABCD) classification system based on exacerbation risk and symptoms in combination with airway limitation
    - However, patients are now classified separately by both their GOLD severity (e.g. airflow limitation: 1 to 4) and exacerbation/symptom assessment (e.g. GOLD grade 4, group D)
    - The definitions of airflow limitation and numerical values for exacerbations/symptoms have not changed, and are summarized below:

Assessment of Airflow Limitation:

- GOLD 1: mild, $FEV_1 \geq 80\%$ predicted
- GOLD 2: moderate, FEV_1 50% to 79% predicted
- GOLD 3: severe, FEV_1 30% to 49% predicted
- GOLD 4: very severe, $FEV_1 < 30\%$ predicted

Assessment of Exacerbation Risk and Symptoms:

- Patient Group A – Low Risk, Less Symptoms: 0 to 1 exacerbations per year (not leading to hospitalization); and CAT score < 10 or mMRC grade 0 to 1
- Patient Group B – Low Risk, More Symptoms: 0 to 1 exacerbations per year (not leading to hospitalization); and CAT score ≥ 10 or mMRC grade ≥ 2
- Patient Group C – High Risk, Less Symptoms: ≥ 2 exacerbations per year or ≥ 1 exacerbation leading to hospitalization; and CAT score < 10 or mMRC grade 0 to 1
- Patient Group D – High Risk, More Symptoms: ≥ 2 exacerbations per year or ≥ 1 exacerbation leading to hospitalization; and CAT score ≥ 10 or mMRC grade ≥ 2

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COPD Agents – Guidelines

- Global Initiative for Chronic Obstructive Lung Disease (GOLD), 2019
  - Recommend treatment plans for COPD based on the aforementioned patient group categories, identified by disease severity (airflow limitation), symptoms, comorbidities and exacerbation/hospitalization risk, although all treatment should be individualized
  - Bronchodilator medications continue to be central to symptom management of COPD across all groups
  - For patients in:
    - **Group A**, a short-acting inhaled bronchodilator ($beta_2$-agonist or antimuscarinics) used on an as-needed basis is recommended as first choice while a long-acting bronchodilator ($beta_2$-agonist or antimuscarinics) are considered as alternatives
    - **Group B**, regular use of a long-acting $beta_2$ agonist (LABA) or long-acting antimuscarinic (LAMA) is recommended, while the combination of a LABA plus a LAMA is an alternative treatment
      - There is insufficient evidence to recommend one long-acting agent over another
    - **Group C**, focus on monotherapy with a long-acting bronchodilator, with preference given to LAMAs
      - If exacerbations persist, then fixed combinations of LABA/LAMA or LABA/inhaled corticosteroids (ICS) may be tried; due to increased risk of pneumonia with ICS agents, a LABA/LAMA combination is preferred
    - **Group D**, prescribers may utilize the same initial therapeutic plan as those in Group C with a goal of reducing exacerbations
      - Initial therapy with a LAMA is recommended as it has effects on both breathlessness and exacerbations. Patients with more severe symptoms (CAT ≥ 20) can be initiated on LABA/LAMA
      - Prescribers may consider a LABA/inhaled corticosteroid (ICS) combination for patients with blood eosinophil counts ≥ 300 cells/mcL as this combination has the greatest likelihood of reducing exacerbations or may be preferred in patients with a history of asthma
      - There is some evidence for use of triple therapy – ICS/LABA/LAMA – in patients with persistent breathlessness or exercise limitation
        - If exacerbations still occur with triple therapy, then the oral phosphodiesterase 4 (PDE4) inhibitor roflumilast (**Daliresp**), which is indicated to decrease the frequency of exacerbations or worsening of symptoms of severe COPD, may be added in patients with an FEV1 of < 50% of predicted and chronic bronchitis
        - Long-term monotherapy with an ICS at any stage has been shown to be less effective than its use in combination with LABAs
        - Following initial therapy, patients should be reassessed for attainment of treatment goals and therapy adjusted as needed

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COPD Agents – Guidelines

- European Respiratory Society (ERS)/ American Thoracic Society (ATS) Joint Guidelines, 2017
  - Recommend long-acting antimuscarinic (LAMA) use over long-acting beta$_2$ agonist (LABA) monotherapy to prevent exacerbations in patients with at least 1 exacerbation during the previous year
  - Suggest treatment with roflumilast to prevent future exacerbations in patients who have COPD with severe or very severe airflow obstruction and symptoms of chronic bronchitis and exacerbations, despite optimal inhaled therapy

Asthma and COPD Agents:
Beta Agonist – Short Acting and Long Acting

Magellan Medicaid Administration

Overview of Disease State – Beta Agonists – Short Acting and Long Acting

- $Beta_2$-agonist bronchodilators are the medications of choice for the treatment and prevention of bronchospasm associated with asthma and prophylaxis of exercise-induced bronchospasm (EIB) in adults and children
  - They are also used in the treatment of chronic obstructive pulmonary disease (COPD)

- In some patients with chronic asthma, a clear distinction between asthma and COPD may be difficult
  - Differing features between asthma and COPD include:
    - The onset of asthma is usually in childhood, while onset of COPD is in mid-life
    - Asthma symptoms vary widely from day to day and are generally worse at night/early mornings, COPD symptoms progress slowly
    - Allergy, rhinitis and/or eczema, as well as obesity are usually present in asthma patients
    - There may be a genetic link with asthma; COPD is generally due to tobacco smoke and occupational pollutants

Overview of Disease State – Beta Agonists – Short Acting and Long Acting

Asthma

- Prevalence of asthma in the United States continues to rise
  - An estimated 7.7% of adults and 8.4% of children (25.2 million Americans) have asthma
  - Further, the National Health Statistics Report shows that asthma appears to disproportionately affect minority groups, females, children, and individuals of low socioeconomic status which can place significant pressure on public health systems
- The National Asthma Education and Prevention Program (NAEPP) of the National Heart Lung and Blood Institute (NHLBI) has defined asthma as a chronic inflammatory disorder of the airways in which many cells and cellular elements play a role
  - In susceptible individuals, inflammation may cause recurrent episodes of wheezing, breathlessness, chest tightness, and coughing
  - These episodes are usually associated with airflow obstruction that is often reversible, either spontaneously or with treatment
  - The inflammation also causes an increase in bronchial hyper-responsiveness to a variety of stimuli.
- Medications to treat asthma are classified as controllers or relievers
  - Controllers are medications taken daily on a long-term basis to maintain asthma control
  - Relievers are medications used on an as-needed basis that act quickly to reverse bronchoconstriction and relieve symptoms
- Short-acting $beta_2$-agonists (SABAs)
  - Have a rapid onset of action and are useful for temporary relief of bronchoconstriction and the accompanying acute symptoms such as wheezing, chest tightness, and cough
  - Have not been shown to be as beneficial as the long-acting controller medications for chronic asthma management
  - Also, increased use of reliever medications is a warning of deterioration in asthma control that indicates a need to reassess treatment

Overview of Disease State – Beta Agonists – Short Acting and Long Acting

COPD

- Pharmacotherapy for COPD is used to decrease symptoms, reduce the frequency and severity of exacerbations and hospitalizations, and improve health status and exercise tolerance
- Bronchodilator medications are central to the symptomatic management of COPD
  - Improve emptying of the lungs, tend to reduce dynamic hyperinflation at rest and during exercise, and improve exercise performance
  - Given either on an as-needed basis for the relief of persistent or worsening symptoms or on a regular basis to prevent or reduce symptoms
  - Regular bronchodilation with these drugs does not modify the decline of function in mild COPD or the prognosis of the disease
  - The principal bronchodilator treatments are beta$_2$-agonists, anticholinergics, and theophylline
    - These may be given either as monotherapy or in combination
  - While SABAs can be used on an as-needed basis in mild COPD, regular treatment with a long-acting agent is required as the disease progresses

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COPD Agents - Beta Agonists – Short Acting – Indications

Drugs	Generic	Reversible Bronchospasm		Prevention of Exercise Induced Broncho-spasm	Chronic Obstructive Pulmonary Disease (COPD)	Age of Use (years)
		Prevention and Treatment	Relief			
Short-Acting Inhalation Agents						
albuterol DPI (ProAir RespiClick)	---	X	X	X	---	≥ 4
albuterol HFA (ProAir® HFA, Proventil HFA, Ventolin HFA)	X	X	X	X	---	≥ 4
albuterol inhalation solution	X	---	X	---	---	≥ 2
albuterol low-dose inhalation solution	X	---	X	---	---	children 2 to 12 years and adolescents
levalbuterol HFA (Xopenex HFA)	X	X	---	---	---	≥ 4
levalbuterol inhalation solution (Xopenex)	X	X	---	---	---	≥ 6
Oral Agents						
albuterol oral syrup	---	---	X	---	---	≥ 2
albuterol oral tablets	X	---	X	---	---	≥ 6
metaproterenol oral syrup	---	X	---	---	X	≥ 6
metaproterenol oral tablets	---	X	---	---	---	≥ 6
terbutaline tablets	X	---	X	---	X	≥ 12

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COPD Agents - Beta Agonists – Short Acting - Dosing and Availability

Drugs	Usual Adult Dosage	Usual Pediatric Dose	Availability
Short-Acting Inhalation Agents			
albuterol DPI (ProAir RespiClick)	Bronchospasm: 2 inhalations every 4 to 6 hours as needed Prevention of EIB: 2 inhalations 15 to 30 minutes prior to exercise	Do not use in patients under 4 years of age	90 mcg per actuation from the mouth piece in a box containing 200 actuations; contains dose counter (breath activated device)†
albuterol HFA (ProAir HFA, Proventil HFA, Ventolin HFA)	Bronchospasm: 2 inhalations every 4 to 6 hours as needed Prevention of EIB: 2 inhalations 15 to 30 minutes prior to exercise	2 inhalations every 4 to 6 hours as needed Prevention of EIB: 2 inhalations 15 to 30 minutes prior to exercise	90 mcg per actuation* from the mouth piece in a canister containing 200 actuations (Proventil HFA, Ventolin HFA and ProAir HFA have dose counters attached to the actuator)
albuterol inhalation solution	2.5 mg every 6 to 8 hours as needed	2 to 12 years of age: 0.1 to 0.15 mg/kg (not to exceed 2.5 mg) nebulized 3 to 4 times a day >12 years of age: 2.5 mg nebulized 3 to 4 times daily	generic: 2.5 mL/0.5 mL (0.5%) and 2.5 mg/3 mL (0.083%) in unit-dose vials; 5 mg/mL in multi-dose bottles low-dose generic: 0.63 mg/3 mL (0.021%) and 1.25 mg/3 mL (0.042%) in unit-dose vials
levalbuterol HFA (Xopenex HFA)	2 inhalations every 4 to 6 hours as needed	2 inhalations every 4 to 6 hours as needed	45 mcg per actuation in a canister containing 200 actuations (with dose counter)
levalbuterol inhalation solution (Xopenex)	0.63 to 1.25 mg 3 times daily	0.31 to 0.63 mg 3 times daily	0.31 mg/3 mL, 0.63 mg/3 mL, 1.25 mg/3 mL, and 1.25 mg/0.5 mL (concentrate) in unit-dose vials

COPD Agents - Beta Agonists – Short Acting - Dosing and Availability

Drugs	Usual Adult Dosage	Usual Pediatric Dose	Availability
		Oral Agents	
albuterol oral syrup	2 to 4 mg every 6 to 8 hours	2 to 6 years of age: 0.1 to 0.2 mg/kg every 8 hours 6 to 12 years of age: 2 mg 3 to 4 times a day	2 mg/5 mL
albuterol oral tablets	Immediate-release: 2 to 4 mg every 6 to 8 hours Extended-release: 8 mg every 12 hours	Immediate-release 6 to 12 years: 2 mg every 6 to 8 hours > 12 years: 2 mg every 6 to 8 hours Extended-release 6 to 12 years of age: 4 mg every 12 hours > 12 years of age: 8 mg every 12 hours	Immediate-release: 2 mg, 4 mg Extended-release: 4 mg, 8 mg‡
metaproterenol oral syrup	20 mg 3 to 4 times daily	10 mg 3 to 4 times daily	10 mg/5 mL
metaproterenol oral tablets	20 mg 3 to 4 times daily	Age 6 – 9 years old or weight < 60 lbs: 10 mg 3 to 4 times daily Age > 9 years old or weight > 60 lbs: 20 mg 3 to 4 times daily	10 mg, 20 mg
terbutaline tablets	2.5 to 5 mg 3 times daily	2.5 mg 3 times daily	2.5 mg, 5 mg

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COPD Agents - Beta Agonists – Long Acting – Indications

Drugs	Generic	Reversible Bronchospasm		Prevention of Exercise Induced Broncho-spasm	Chronic Obstructive Pulmonary Disease (COPD)	Age of Use (years)
		Prevention and Treatment	Relief			
Short-Acting Inhalation Agents						
arformoterol inhalation solution (Brovana)	---	---	---	---	X	≥ 18
formoterol inhalation solution (Perforomist)	---	---	---	---	X	≥ 18
indacaterol inhalation powder (Arcapta Neohaler)	---	---	---	---	X	≥ 18
olodaterol inhalation spray (Striverdi Respimat)	---	---	---	---	X	≥ 18
salmeterol DPI (Serevent Diskus)	---	X	---	X	X	≥ 4

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COPD Agents - Beta Agonists – Long Acting - Dosing and Availability

Drugs	Usual Adult Dosage	Prevention of EIB	Usual Pediatric Dose	Availability
Long Acting Inhalation Agents				
arformoterol inhalation solution (Brovana)	15 mcg twice daily	---	---	15 mcg/2 mL inhalation solution
formoterol inhalation solution (Perforomist)	20 mcg every 12 hours	---	---	20 mcg/2 mL inhalation solution
indacaterol inhalation powder (Arcapta Neohaler)	75 mcg inhaled once daily using the Neohaler inhaler	---	---	75 mcg capsules in aluminum blister cards (breath activated device)
olodaterol inhalation spray (Striverdi Respimat)	2 inhalations once daily	---	---	2.5 mcg per inhalation
salmeterol DPI (Serevent Diskus)	1 inhalation every 12 hours	1 inhalation 30 minutes before exercise; not to administer a second dose within 12 hours	Ages 4 years and up: 1 inhalation every 12 hours	50 mcg per inhalation (breath activated device)

COPD Agents - Beta Agonists – Short Acting – Guidelines

- Global Initiative for Asthma (GINA), 2019
  - Offer a management plan to adjust treatment in a continuous cycle of assessment, treatment, and review of the patient's response as it relates to symptom control, future risk of exacerbations, and side effects
  - During this continuous cycle, a stepwise treatment approach is used to achieve control using the patient's current level of control as the baseline
    - If the patient is not controlled on the current regimen, treatment should be stepped up until control is achieved
  - According to GINA's stepwise approach, patients in steps 1 and 2 are considered to have mild asthma, patients in step 3 to 4, moderate asthma, and patients in steps 4 and 5, moderate to severe asthma
  - The 2019 GINA guidelines recommend that all adults and adolescents with asthma receive an ICS-containing controller medication
  - Due to the increased risk of severe exacerbations and asthma-related death, short-acting beta agonist (SABA)-only treatment is no longer recommended
  - For most asthma patients, treatment can be initiated with an as-needed low dose ICS-formoterol (step 1) or daily low dose ICS (step 2)
  - In patients whose asthma is uncontrolled on a low-dose ICS-containing controller despite good adherence and correct technique, a step up in treatment may be added (see tables on next slide)
    - Any step up in therapy should be re-assessed after 2 to 3 months; if there is not an adequate response, consider alternative treatment options or a referral
    - If asthma control is maintained for at least 3 months on the current regimen, treatment can be stepped down to the lowest step and dosage that maintains control

COPD Agents - Beta Agonists – Short Acting – Guidelines

- Global Initiative for Asthma (GINA), 2019
  - Severe asthma is uncontrolled asthma despite adherence with optimized step 4 or step 5 treatment, correct inhaler technique, and proper management of contributory factors or asthma that worsens when high dose therapy is decreased
  - If asthma is uncontrolled after 3 to 6 months on high dose ICS-LABA, it is recommended to refer to a specialist and phenotype into categories, such as severe allergic, aspirin-exacerbated, or eosinophilic asthma, as this may guide the selection of add-on treatment
    - Add-on treatments for severe asthma include tiotropium (Spiriva), low-dose azithromycin (off-label), a leukotriene receptor antagonist (LTRA), a monoclonal antibody (benralizumab [**Fasenra**], mepolizumab [**Nucala**], omalizumab [**Xolair**], dupilumab [**Dupixent**]), a low-dose oral corticosteroid (OCS), bronchial thermoplasty, or sputum-guided therapy
      - Patients with severe allergic asthma with elevated immunoglobulin E (IgE) levels may benefit from Xolair (anti-IgE) therapy (Evidence A)
      - Those with severe eosinophilic asthma may benefit from Fasenra, Nucala, and Cinqair (anti-IL-5) therapy (Evidence A)
      - Those with severe eosinophilic/Type 2 asthma or patients requiring maintenance OCS may benefit from Dupixent (anti-IL-4) therapy (Evidence A)
      - Those with aspirin sensitivity may benefit from leukotriene receptor antagonists (LTRA) (Evidence B)

COPD Agents - Beta Agonists – Short Acting – Guidelines

- Global Initiative for Asthma (GINA), 2019 – Controller Therapy

Step	Age Group	Preferred Controller	Other Controller Options
Step 1: Symptom-driven or regular controller	≥ 12 years	▪ As-needed low dose ICS-formoterol (unlabeled indication)	▪ Low dose ICS whenever SABA is taken (unlabeled indication)
	6 to 11 years	--	▪ Low dose ICS whenever SABA is taken (unlabeled indication) or daily low dose ICS
Step 2: One controller AND an as-needed reliever medication	≥ 12 years	▪ Low dose ICS or as needed low dose ICS-formoterol (unlabeled indication)†	▪ Leukotriene modifier or low dose ICS whenever SABA is taken (unlabeled indication)
	6 to 11 years	▪ Low dose ICS	▪ Leukotriene modifier or low dose ICS whenever SABA is taken (unlabeled indication)
Step 3: Two controllers and an as-needed reliever medication	≥ 12 years	▪ Low dose ICS/LABA	▪ Medium dose ICS OR low dose ICS + leukotriene modifier ▪ Sublingual immunotherapy (SLIT) may be considered in adults with allergic rhinitis, house dust mite sensitivity, and FEV > 70% predicted
	6 to 11 years	▪ Low dose ICS/LABA or medium dose ICS	▪ Low dose ICS + leukotriene modifier

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COPD Agents - Beta Agonists – Short Acting – Guidelines

- Global Initiative for Asthma (GINA), 2019 – Controller Therapy

Step	Age Group	Preferred Controller	Other Controller Options
Step 4: Two controllers and an as-needed reliever medication	≥ 12 years	▪ Medium dose ICS/LABA	▪ High dose ICS, add-on tiotropium, or add-on leukotriene modifier ▪ Sublingual immunotherapy (SLIT) may be considered in adults with allergic rhinitis, house dust mite sensitivity, and FEV > 70% predicted
	6 to 11 years	▪ Medium dose ICS/LABA; refer for expert advice	▪ High dose ICS/LABA, add-on tiotropium, or add-on leukotriene modifier
Step 5: Two controllers and an as-needed reliever medication	≥ 12 years	▪ High dose ICS/LABA; refer for phenotypic assessment with or without add-on therapy (e.g., tiotropium, anti-IgE [omalizumab], anti-interleukin-5[IL5]/5R [mepolizumab, reslizumab, benralizumab], anti-IL4R [dupilumab])	▪ Add-on low dose oral corticosteroid, considering adverse effects
	6 to 11 years	▪ **Refer for phenotypic assessment with or without add-on therapy (e.g., anti-IgE [omalizumab)**	▪ **Add-on anti-IL-5 or add-on low dose oral corticosteroid, considering adverse effects**

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COPD Agents - Beta Agonists – Short Acting – Guidelines

- Global Initiative for Asthma (GINA), 2019 – Reliever Therapy

Step	Age Group	Preferred Reliever	Other RelieverOptions
≥ 12 years	Steps 1 and 2	▪ As-needed low dose ICS-formoterol (unlabeled indication)	▪ As needed SABA
	Steps 3 through 5	▪ As-needed low dose ICS-formoterol (unlabeled indication)	
6 to 11 years	Steps 1 through 5	▪ As needed SABA	--

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COPD Agents - Beta Agonists – Short Acting – Guidelines

- National Asthma Education and Prevention Program (NAEPP), 2007
  - Emphasizes the importance of asthma control, and identifies asthma severity as the intrinsic intensity of the disease process
  - The EPR-3 advises of the need to first assess severity as the basis of initial therapy and then assess control to adjust therapy

  - Short Acting Beta Agonists (SABA)
    - Recommend that inhaled SABAs are the drugs of choice for treating acute asthma symptoms and exacerbations and for preventing exercise induced bronchospasm (EIB)
    - Regularly scheduled, daily, chronic use of a SABA is not recommended
    - Use of a short-acting agent greater than 2 days per week for symptom relief is indicative of inadequate asthma control and the need for a step-up in treatment (i.e. anti-inflammatory medication should be started or intensified)
    - The inhaled route is preferred due to faster onset of action, fewer adverse effects, and increased efficacy
    - Agents less selective for the $beta_2$ receptor, including metaproterenol, are not recommended due to excessive cardiac stimulation

Asthma and COPD Agents: Inhaled Corticosteroids

Magellan Medicaid Administration

Asthma and COPD Agents – Inhaled Corticosteroids- Indications

Drugs	Generic	Indication(s)
Glucocorticoids		
beclomethasone HFA inhalation aerosol (QVAR Redihaler)	---	• Maintenance treatment of asthma as prophylactic therapy (see indicated ages below for each product) **Indicated Ages** • QVAR Redihaler is for use in patients age 4 years and older • Pulmicort Flexhaler is for use in patients age 6 years and older • Pulmicort Respules are used in patients age 12 months to 8 years • Flovent HFA and Flovent Diskus are for use in patients age 4 years and older • Asmanex Twisthaler is for use in patients age 4 years and older • Aerospan is for use in patients 6 years and older • Arnuity Ellipta is for use in patients 5 years and older • Alvesco, ArmonAir RespiClick, and Asmanex HFA are for adult and adolescent patients 12 years of age
budesonide inhalation powder (Pulmicort Flexhaler)	---	
budesonide inhalation suspension (Pulmicort Respules)	**X**	
ciclesonide inhalation aerosol (Alvesco)	---	
flunisolide HFA (Aerospan)	---	
fluticasone furoate inhalation powder (Arnuity Ellipta)	---	
fluticasone propionate inhalation aerosol (Flovent HFA)	---	
fluticasone propionate inhalation powder, (ArmonAir RespiClick)	---	
fluticasone propionate inhalation powder (Flovent Diskus)	---	
mometasone furoate inhalation aerosol (Asmanex HFA)	---	
mometasone furoate inhalation powder (Asmanex Twisthaler)	---	

Asthma and COPD Agents – Inhaled Corticosteroids- Indications

Drugs	Generic	Indication(s)
Glucocorticoid/Long-Acting Beta2-Agonist (LABA) Combinations		
budesonide/formoterol inhalation aerosol (Symbicort)	---	▪ Treatment of asthma in patients 6 years of age and older ▪ Maintenance treatment of airflow obstruction in patients with COPD including chronic bronchitis and emphysema
fluticasone furoate/vilanterol (Breo Ellipta)	---	▪ Long-term, once daily, maintenance treatment of airflow obstruction in patients with COPD, including chronic bronchitis and/or emphysema ▪ To reduce exacerbations of COPD in patients with a history of exacerbations ▪ Treatment of asthma in patients 18 years of age and older
fluticasone propionate/ salmeterol inhalation aerosol (Advair HFA)	---	▪ Treatment of asthma in patients 12 years of age and older
fluticasone propionate/ salmeterol inhalation powder (Advair Diskus)	X	▪ Treatment of asthma in patients 4 years of age and older ▪ Maintenance treatment of airflow obstruction in COPD including chronic bronchitis and emphysema (250/50 mcg only) ▪ To reduce COPD exacerbations in patients with a history of exacerbations (250/50 mcg only)
fluticasone propionate/ salmeterol inhalation powder (AirDuo RespiClick)	---	▪ Treatment of asthma in patients 12 years of age and older
mometasone/formoterol inhalation aerosol (Dulera)	---	▪ Treatment of asthma in patients 12 years of age and older
Glucocorticoid/Long-Acting Anticholinergic/Long-Acting Beta2-Agonist (LABA) Combinations		
fluticasone furoate/ umeclidinium/vilanterol (Trelegy Ellipta)	---	▪ Maintenance treatment of COPD

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Asthma and COPD Agents – Inhaled Corticosteroids- Dosing and Availability

Drugs	Adult Dosage		Pediatric Dose		Availability
	Initial	Maximum	Initial	Maximum	
Glucocorticoids					
beclomethasone HFA inhalation aerosol (QVAR Redihaler)	40 mcg to 80 mcg twice daily (previous bronchodilator use alone); 40 mcg to 320 mcg twice daily (previous inhaled corticosteroid therapy)	320 mcg twice daily	Age 4 to 11 years: 40 mcg twice daily (Use adult dosing for ages ≥ 12 years)	Age 4 to 11 years: 80 mcg twice daily	40 mcg and 80 mcg breath activated MDI (120 actuations per 10.6 g canister) Dose counter available for all strengths
budesonide inhalation powder (Pulmicort Flexhaler)	360 mcg twice daily	720 mcg twice daily	Age 6 to 17 years: 180 mcg twice daily	Age 6 to 17 years: 360 mcg twice daily	90 mcg and 180 mcg DPI (60 mcg and 120 actuations per canister, respectively) Dose counter available for all strengths Breath activated device
budesonide inhalation suspension (Pulmicort Respules)	--	--	Age 12 months to 8 years: Prior bronchodilator alone: 500 mcg once daily or 250 mcg twice daily Prior ICS: 500 mcg once daily or 250 mcg to 500 mcg twice daily Prior oral glucocorticoid: 500 mcg twice daily or 1,000 mcg once daily	--	250 mcg, 500 mcg, and 1,000 mcg per 2 mL Respules via jet nebulizer

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Asthma and COPD Agents – Inhaled Corticosteroids- Dosing and Availability

Drugs	Adult Dosage		Pediatric Dose		Availability
	Initial	Maximum	Initial	Maximum	
Glucocorticoids					
ciclesonide inhalation aerosol (Alvesco)	80 mcg twice daily (patients who received bronchodilator alone)	160 mcg twice daily	Age 12 years and older: 80 mcg twice daily (patients who received bronchodilator alone)	Age 12 years and older: 160 mcg twice daily	80 mcg and 160 mcg MDI with HFA propellant (60 actuations per 6.1 g canister) Dose counter available for all strengths
	80 mcg twice daily (patients who received inhaled corticosteroid)	320 mcg twice daily	Age 12 years and older: 80 mcg twice daily (patients who received inhaled corticosteroid)	Age 12 years and older: 320 mcg twice daily	
	320 mcg twice daily (patients who received oral corticosteroids)	320 mcg twice daily	Age 12 years and older: 120 mcg twice daily (patients who received oral corticosteroid)	Age 12 years and older: 320 mcg twice daily	
flunisolide HFA inhalation aerosol (Aerospan)	160 mcg twice daily (without prior inhaled corticosteroid); 160 mcg to 320 mcg twice daily (prior inhaled corticosteroid)	320 mcg twice daily*	80 mcg twice daily (without prior inhaled corticosteroid); 80 mcg to 160 mcg twice daily (prior inhaled corticosteroid)	160 mcg twice daily*	80 mcg MDI with HFA propellant (120 actuations per 8.9 g canister)
fluticasone furoate inhalation powder (Arnuity Ellipta)	One Inhalation of 100 mcg or 200 mcg once daily (starting dose based on prior asthma therapy and disease severity)	200 mcg daily	Age 5 to 11 years: 50 mcg once daily Age 12 years and older: 100 mcg (initial) to 200 mcg once daily	Age 5 to 11 years: 50 mcg daily Age 12 years and older: 200 mcg daily	50 mcg, 100 mcg, and 200 mcg blister strip of powder for inhalation (each package contains 30 blisters) Breath activated device

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Asthma and COPD Agents – Inhaled Corticosteroids- Dosing and Availability

Drugs	Adult Dosage		Pediatric Dose		Availability
	Initial	Maximum	Initial	Maximum	
Glucocorticoids					
fluticasone propionate inhalation aerosol (Flovent HFA)	88 mcg twice daily (without prior inhaled corticosteroid); 88–880 mcg twice daily (prior inhaled corticosteroid)	880 mcg twice daily	Age 4 to 11 years: 88 mcg twice daily	Age 4 to 11 years: 88 mcg twice daily	44 mcg, 110 mcg, and 220 mcg MDI with HFA propellant (120 actuations per canister) Dose counter available for all strengths
fluticasone propionate inhalation powder (ArmonAir RespiClick)	55 mcg twice daily (55 mcg to 232 mcg twice daily may be used in patients transitioning from other ICS products)	232 mcg twice daily	Age 12 years and older: 55 mcg twice daily (55 mcg to 232 mcg twice daily may be used in patients transitioning from other ICS products)	Age 12 years and older: 55-232 mcg twice daily	55 mcg and 232 mcg (delivers 51 mcg and 210 mcg of fluticasone, respectively) in inhaler devices containing 60 doses each Dose counter available for all strengths Breath activated device
fluticasone propionate inhalation powder (Flovent Diskus)	100 mcg twice daily (patients who received bronchodilators alone)	500 mcg twice daily	Age 4 to 11 years: 50 mcg twice daily (when prior therapy is with bronchodilator alone or inhaled corticosteroid)	Age 4 to 11 years: 100 mcg twice daily	50 mcg, 100 mcg, and 250 mcg blister units (60 blisters per pack) Dose counter available for all strengths Breath activated device
	100 mcg to 250 mcg twice daily (patients who used ICS)	500 mcg twice daily			
	500 mcg to 1,000 mcg twice daily (patients who used oral	1,000 mcg twice daily			

Asthma and COPD Agents – Inhaled Corticosteroids- Dosing and Availability

Drugs	Adult Dosage		Pediatric Dose		Availability
	Initial	Maximum	Initial	Maximum	
Glucocorticoids					
mometasone furoate inhalation aerosol (Asmanex HFA)	Based on prior asthma therapy: 2 inhalations of 100 mcg or 200 mcg twice daily	400 mcg twice daily	Age 12 years and older: 2 inhalations of 100 mcg or 200 mcg twice daily	Age 12 years and older: 400 mcg twice daily	100 mcg and 200 mcg pressurized MDI (120 actuations per unit)
mometasone furoate inhalation powder (Asmanex Twisthaler)	220 mcg daily in evening (if on bronchodilator alone or inhaled corticosteroid) or 440 mcg twice daily (if on oral corticosteroid)	440 mcg daily (single or divided doses) or 880 mcg daily	Age 12 years and older: 220 mcg daily in evening (if on bronchodilator alone or inhaled steroid) or 440 mcg twice daily (if on oral corticosteroid) Age 4 to 11 years of age: 110 mcg once daily in the evening	Age 12 years and older: 440 mcg daily (single or divided doses) or 880 mcg daily Age 4 to 11 years of age: 110 mcg once daily in the evening	110 mcg and 220 mcg DPI (110 mcg: 30 actuations per unit; 220 mcg: 30, 60, or 120 actuations per unit) Dose counter available for all strengths Breath activated device
budesonide/formoterol inhalation aerosol (Symbicort)	Asthma: 2 inhalations twice daily of 80/4.5 mcg or 160/4.5 mcg COPD: 2 inhalations twice daily of 160/4.5 mcg	2 inhalations twice daily of 160/4.5 mcg	Age 6 years to 11 years (asthma): 2 inhalations twice daily of 80/4.5 mcg Age 12 years and older (asthma): 2 inhalations twice daily of 80/4.5 mcg or 160/4.5 mcg	Age 12 years and older: 2 inhalations twice daily of 160/4.5 mcg	80/4.5 mcg and 160/4.5 mcg per actuation MDI with HFA propellant (60 or 120 actuations per canister) Dose counter available for all strengths

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Asthma and COPD Agents – Inhaled Corticosteroids- Dosing and Availability

Drugs	Adult Dosage		Pediatric Dose		Availability
	Initial	Maximum	Initial	Maximum	
Glucocorticoids					
fluticasone furoate/vilanterol inhalation powder (Breo Ellipta) **The recommended starting dosages for asthma are based on prior asthma therapy (ICS)**	Asthma: Low-to mid-dose ICS: 1 inhalation of 100/25 mcg once daily Mid- to high-dose ICS: 1 inhalation of 200/ 25 mcg once daily COPD: 1 inhalation of 100/25 mcg once daily	Asthma: 1 inhalation of 200/25 mcg once daily COPD: 1 inhalation of 100/25 mcg once daily	--	--	100/25 mcg and 200/25 mcg per inhalation (60 actuations per unit) Dose counter available Breath activated device
fluticasone propionate/salmeterol inhalation aerosol (Advair HFA)	2 inhalations of 45/21 mcg twice daily or 115/21 mcg twice daily or 230/21 mcg twice daily	2 inhalations of 230/21 mcg twice daily	Age 12 years and older: 2 inhalations of 45/21 mcg twice daily or 115/ 21 mcg twice daily or 230/21 mcg twice daily	Age 12 years and older: 2 inhalations of 230/ 21 mcg twice daily	45/21 mcg, 115/21 mcg, and 230/21 mcg per actuation MDI with HFA propellant (60 or 120 actuations per canister) Dose counter available for all strengths
fluticasone propionate/salmeterol inhalation powder (Advair Diskus)	Asthma: 100/50 mcg twice daily to 500/50 mcg twice daily Maintenance treatment of COPD: 1 inhalation twice daily of 250/50 mcg	Asthma: 500/50 mcg twice daily	Age 4 to 11 years: 100/50 mcg twice daily Age 12 years and older: 1 inhalation twice daily of 100/50, 250/50, or 500/50 mcg	--	100/50 mcg, 250/50 mcg, and 500/50 mcg per actuation Diskus DPI† (60 blisters/actuations per unit) Dose counter available for all strengths Breath activated device

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Asthma and COPD Agents – Inhaled Corticosteroids- Dosing and Availability

Drugs	Adult Dosage		Pediatric Dose		Availability
	Initial	Maximum	Initial	Maximum	
Glucocorticoids					
fluticasone propionate/salmeterol inhalation powder (AirDuo RespiClick)	Asthma: 1 inhalation (55/14 mcg to 232/14 mcg) twice daily	Asthma: 232/14 mcg twice daily	Age 12 years and older: 1 inhalation (55/14 mcg to 232/14 mcg) twice daily	Age 12 years and older: 1 inhalation (55/14 mcg to 232/14 mcg) twice daily	55/14 mcg, 113/14 mcg and 232/14 mcg per actuation (60 actuations per unit) Dose counter available for all strengths Breath activated device Not to be used with a spacer or holding chamber
mometasone/formoterol inhalation aerosol (Dulera) **The recommended starting dosages are based on prior asthma therapy**	For medium dose ICS: 2 inhalations of 100/5 mcg twice daily For high dose ICS: 2 inhalations of 200/5 mcg twice daily	Dose ICS: 2 inhalations of 100/5 mcg twice daily For high dose ICS: 2 inhalations of 200/5 mcg twice daily	Age 12 years and older: For medium dose ICS: 2 inhalations of 100/5 mcg twice daily For high dose ICS: 2 inhalations of 200/5 mcg twice daily	Age 12 years and older: For medium dose ICS: 2 inhalations of 100/5 mcg twice daily For high dose ICS: 2 inhalations of 200/5 mcg twice daily	100/5 mcg and 200/5 mcg per actuation (120 actuations per unit) MDI Dose counter available for all strengths
fluticasone furoate/ umeclidinium/vilanterol (Trelegy Ellipta)	1 inhalation once daily at the same time each day	1 inhalation once daily at the same time each day	--	--	100/62.5/25 mcg per actuation DPI (30 actuations per unit) with dose counter Supplied as inhalation powder in 2 foil blister strips per actuation (1 containing fluticasone furoate, 1 containing umeclidinium/vilanterol) Breath activated device

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Antipsoriatics, Oral

Overview of Disease State – Antipsoriatics

- **Psoriasis**
  - A common chronic, inflammatory, multisystem condition, with predominantly skin and joint (arthritis) manifestations
  - It is characterized by erythematous plaques and plaques with silvery scales which negatively impacts quality of life
  - It is estimated that over 8 million people in the United States (US) have psoriasis
    - The prevalence of psoriasis is 1.9% in African Americans, about 1% of Hispanics, and 3.6% in Caucasians
    - It usually presents between the ages of 15 to 35 years, but psoriasis can develop at any age
  - There are 5 types of psoriasis:
    - Plaque, guttate, inverse, pustular, and erythrodermic
    - The most common type is plaque psoriasis (psoriasis vulgaris) in which patches or lesions of skin become inflamed and is covered by a silvery white scale
    - The plaques frequently occur on the skin of the elbows and knees but can affect any area, including the scalp
- Mild to moderate psoriasis
  - Generally treated with topical agents
  - Phototherapy is used when the disease is widespread or unresponsive to topical agents
  - Systemic agents, including biologic drugs, are usually reserved for patients with moderate to severe disease or those with psoriatic arthritis
- Moderate to severe psoriasis
  - Defined as involvement of more than 5% to 10% of the body surface area or involvement of the face, palm or sole, or disease that is otherwise disabling
  - Patients with moderate to severe disease are generally candidates for systemic therapy
  - Options for systemic therapy include methotrexate, cyclosporine, retinoids (acitretin), biologics, and methoxsalen plus ultraviolet A (UVA) radiation

Antipsoriatics, Oral – Indications

Drugs	Generic	Indications
acitretin (Soriatane)	**X**	Treatment of severe psoriasis in adults
methoxsalen (Oxsoralen-Ultra)	**X**	Photochemotherapy (methoxsalen with long wave UVA radiation) is indicated for the symptomatic control of severe, recalcitrant, disabling psoriasis not adequately responsive to other forms of therapy and when the diagnosis has been supported by biopsy Methoxsalen is intended to be administered only in conjunction with a schedule of controlled doses of long wave ultraviolet radiation

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Antipsoriatics, Oral – Dosing and Availability

Drug	Dose	Availability
acitretin (Soriatane)	Initial: 25 mg to 50 mg orally once daily with the main meal Maintenance: doses of 25 mg to 50 mg/day orally may be given dependent upon an individual's response to initial treatment	10 mg, 17.5 mg (generic only), and 25 mg gelatin capsules Protect from light
methoxsalen (Oxsoralen-Ultra)	Initiate therapy 1.5 to 2 hours prior to UVA with low fat food or milk, based on the drug's weight-based dosing table	10 mg soft gelatin capsule

Antipsoriatics, Oral – Guidelines

The American Academy of Dermatology (AAD), 2009

- The 2009 AAD systemic therapy guidelines for psoriasis note that Soriatane, methotrexate, and cyclosporine have been used for the treatment of psoriasis for many years with good to excellent results (strength of recommendation B; level of evidence II)
- However, of the systemic therapies, Soriatane is the least effective monotherapy
  - Therefore, it is used often in conjunction with ultraviolet B (UVB) or psoralen plus UVA (PUVA) phototherapy
- Soriatane
  - Like the other retinoids, appears to be more efficacious in the inflammatory forms of psoriasis
  - Has been used as maintenance therapy; after 6 and 12 months of continuous treatment, 75% and 88% of patients, respectively, with chronic plaque psoriasis reached a Psoriasis Area Severity Index (PASI) 50
  - May be combined with tumor necrosis factor-α (TNF-α) inhibitors (e.g., adalimumab, etanercept, infliximab, ustekinumab) to augment therapy with negligible immunosuppressive effects
  - Due to lack of significant immunosuppression, Soriatane is generally considered the treatment of choice in human immunodeficiency virus (HIV)-positive patients with severe psoriasis
- UV Light Therapy
  - Although treatment options for psoriasis have expanded in recent years, UV light therapy remains a therapeutic option for patients
  - Phototherapy generally lacks the systemic immunosuppressive properties of both traditional and biologic systemic therapies
  - Psoralen plus PUVA photochemotherapy combines administration of psoralens, a class of phototoxic compounds, with an exposure to ultraviolet A radiation (UVA) under strict medical supervision
  - UVA penetrates deeper into the dermis than UVB and does not have UVB's potential for skin burning. The 2010 AAD systemic therapy guidelines for psoriasis with phototherapy and photochemotherapy, recommend oral PUVA (strength of recommendation A; level of evidence I)

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Dermatologics: Antipsoriatics, Topical

Antipsoriatics, Topical – Indications

Drugs	Generic	Indications	
		Plaque psoriasis (psoriasis vulgaris)	Psoriasis of scalp
calcipotriene cream (Dovonex)	X	X	--
calcipotriene foam (Sorilux)	--	X	X
calcipotriene ointment (Calcitrene)	X	X	--
calcipotriene solution	X	--	X
calcipotriene/betamethasone foam (Enstilar)	--	X	--
calcipotriene/betamethasone ointment (Taclonex)	X	X (≥ 12 years)	--
calcipotriene/betamethasone topical suspension (Taclonex)	--	X	X (≥ 12 years)
calcitriol (Vectical)	X	X	--
tazarotene (Tazorac)	X	X	--
tazarotene/ halobetasol propionate (Duobrii)	--	X	--

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Antipsoriatics, Topical – Dosing and Availability

Drugs	Adult	Children ≥ 12 years	Availability
calcipotriene (Dovonex)	Apply twice daily for 8 weeks	--	0.005% cream: 60 g, 120 g tube 0.005% solution: 60 mL bottle (generic only)
calcipotriene (Calcitrene)	Apply once to twice daily	--	0.005% ointment: 60 g, 120 g tube
calcipotriene (Sorilux)	Apply twice daily	Apply twice daily	0.005% foam: 60 g, 120 g canister
calcipotriene/betamethasone (Enstilar)	Apply once daily for up to 4 weeks; do not used more than 60 grams every 4 days	--	0.005%/0.064% topical foam: 60 g in an canister in packages of 1 or 2 canisters
calcipotriene/betamethasone (Taclonex)	Ointment: apply once daily for up to 4 weeks Suspension: apply once daily for up to 8 weeks Weekly dose should not exceed 100 grams	Apply once daily for up to 4 weeks (ointment) or 8 weeks (suspension); Weekly dose should not exceed 60 grams	Calcipotriene/betamethasone 0.005%/0.064% ointment: 60 g, 100 g tube Calcipotriene/betamethasone 0.005%/0.064% topical suspension: 60 g, 120 g bottle
calcitriol (Vectical)	Apply to the affected areas twice daily; Maximum weekly dose should not exceed 200 grams	--	3 mcg/gm ointment: 100 g tube
tazarotene (Tazorac)	Apply once daily in the evening	Apply tazarotene gel once daily	0.05% (brand only) and 0.1% cream: 30 g tube, 60 g jar/tube 0.05% and 0.1% gel: 30 g, 100 g jar (brand only)
tazarotene/halobetasol propionate (Duobrii)	Apply to affected areas once daily Do not exceed 50 g/week	--	tazarotene/halobetasol propionate 0.045%/0.01% lotion: 100 g jar

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Antipsoriatics, Topical – Guidelines

The American Academy of Dermatology (AAD)

- Traditionally, pharmacotherapy choices include emollients, topical corticosteroids, phototherapy, and systemic medications
- Approximately 80% of patients affected with psoriasis have mild to moderate disease that can be managed with topical agents and emphasizes the importance of tailoring treatment options to meet individual patients' needs
- Topical corticosteroids remain the cornerstone of treatment for most patients with psoriasis, especially for those with limited disease, and the wide availability of strengths and formulations allow for versatility of use

- However, limitations exist with topical steroid use
  - The clinical data available for the safety and efficacy of topical corticosteroids report a short duration of use, approximately 2 to 4 weeks, and treatment extending beyond this time period increases the risk of cutaneous adverse effects and systemic absorption
  - Both systemic and local cutaneous adverse effects are a concern with extensive use of corticosteroids, such as telangiectasia (capillary dilation at the skin surface), striae distensae, acne, folliculitis, and purpura
  - As a result, despite the corticosteroids being the mainstay of topical treatment, the most potent and efficacious agents are only approved for short-term treatment, approximately 2 to 4 weeks

National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS)

- Advises the use of topical steroids helps to improve psoriasis, but does not eliminate the disease
- Often times the affected skin will become resistant to the topical steroid requiring use of an alternative agent
- Furthermore, rebound exacerbation of the disease has been reported with abrupt discontinuation of the corticosteroid; therefore, tapering is recommended, but guidance is lacking on details of tapering

Antipsoriatics, Topical – Guidelines

The National Psoriasis Foundation 2017 Guideline Update

- Advises on the treatment of inverse or intertriginous psoriasis, which typically affects skin fold areas such as axilla, perianal skin, intergluteal cleft, inframammary, genital/inguinal, abdominal, and retroauricular folds
- They state that while low-potency topical corticosteroids may be appropriate for short-term use, long-term therapy includes topical calcitriol, calcipotriene, and immunomodulators
- Antimicrobials, emollients, and coal-tar products are considered second or third-line treatments
- For resistant inverse psoriasis, botulinum toxin, laser therapy, and select anti-tumor necrosis factor agents or anti-interleukin 12/23 treatment are recommended
- An updated consensus guidelines of care for the management of psoriasis with topicals by the AAD and NPF is expected in the first quarter of 2020

Immunomodulators, Topical

Magellan Medicaid Administration

Overview of Disease State – Immunomodulators, Topical

- Actinic Keratosis (AK)
  - A premalignant condition of the skin that manifests as small, thick, scaly patches of the skin
  - It is seen mostly in sun-exposed areas of the skin and should be treated due to its potential to progress into a squamous cell carcinoma (SCC)

- Genital Warts
  - According to the Centers for Disease Control and Prevention (CDC), about 79 million Americans are currently infected with human papilloma virus (HPV) and 14 million people become newly infected each year
  - Due to its prevalence and the likelihood of transmission in sexually active patients, the CDC encourages vaccination in recommended age groups
  - Genital warts are typically caused by HPV types 6 or 11 in 90% of occurrences
  - Genital warts are usually flat, papular, or pedunculated growths on the genital mucosa
  - No evidence indicates that the presence of genital warts or their treatment is associated with the development of cervical cancer

- Treatment
  - Patient-applied topical treatments for genital and perianal warts include imiquimod, podofilox, and sinecatechins
    - Imiquimod stimulates production of interferon and other cytokines
    - Podofilox is a plant-based antimitotic agent
    - Sinecatechins is a green tea extract that may treat genital and perianal warts via anti-oxidative affects

Immunomodulators, Topical – Indications

Drugs	Generic	Indications
imiquimod (Aldara)	X	Clinically typical, nonhyperkeratotic, nonhypertrophic actinic keratoses on the face or scalp in immunocompetent adults
		Biopsy-confirmed, primary superficial basal cell carcinoma (sBCC) in immunocompetent adults; maximum tumor diameter of 2.0 cm on trunk, neck, or extremities (excluding hands and feet), only when surgical methods are medically less appropriate and patient follow-up can be reasonably assured
		External genital and perianal warts/condyloma acuminata in patients 12 years or older
imiquimod (Zyclara)	---	Clinically typical, visible, or palpable actinic keratoses of the full face or balding scalp in immunocompetent adults
		External genital and perianal warts/condyloma acuminata in patients 12 years or older
podofilox gel (Condylox)	---	• Treatment of external genital warts (Condyloma acuminatum) • Podofilox is not indicated in the treatment of perianal or mucous membrane warts
podofilox solution	X	
sinecatechins (Veregen)	---	• Treatment of external genital and perianal warts (Condylomata acuminata) in immunocompetent patients ≥ 18 years old • Safety and efficacy of use beyond 16 weeks or for multiple treatment courses has not been established

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Immunomodulators, Topical – Dosing and Availability

Drugs	Dosage	Availability
imiquimod (Aldara)	▪ Actinic keratosis: apply two times per week for a full 16 weeks	5% cream, supplied in single-use packets which contain 250 mg of the cream
	▪ Superficial basal cell carcinoma: apply five times per week for a full six weeks	
	▪ External genital warts: apply three times per week until total clearance or a maximum of 16 weeks	
imiquimod (Zyclara)	▪ Actinic keratosis: apply once daily to the skin of the affected area (either the entire face or balding scalp) for two 2-week treatment cycles separated by a 2-week no-treatment period	2.5% or 3.75% cream, supplied in single-use packets which contain 250 mg of the cream or 30 mL pump bottles
	▪ External genital warts: apply once daily to the external genital/perianal warts until total clearance or up to eight weeks	
podofilox gel (Condylox)	▪ Apply every 12 hours for 3 consecutive days, then withhold use for 4 consecutive days; repeat this 7-day regimen up to 4 times until there is no visible wart	0.5% gel in 3.5 gm
podofilox solution		0.5% solution in 3.5 mL
sinecatechins (Veregen)	▪ Apply 3 times per day until complete clearance for up to 16 weeks	15% ointment in 30 gram tube

Immunomodulators, Topical – Guidelines

- **Actinic Keratosis (AK)**
  - There are no widely accepted guidelines for the treatment of AK published in the United States
  - British Association of Dermatologists, 2007
    - The treatment options below are listed along with their associated strength of recommendation and quality of evidence rating:
      - No therapy (A,ll-ii) (for mild AK)
      - Sun block (SPF 16) applied twice daily for 7 months (A,I)
      - 5-fluorouracil applied twice daily for 6 weeks (A,I)
      - Topical diclofenac 3% (B,I)
      - Tretinoin cream (B,I)
      - Imiquimod 5% cream (B,I)
  - International League of Dermatological Societies, European Dermatology Forum
    - For single lesions
      - Suggest the use of imiquimod 3.75% or 5%
    - Multiple lesions
      - Recommend 3.75% imiquimod
      - Suggest the use of 2.5% or 5% imiquimod
- **Genital Warts**
  - The CDC's 2015 guidelines recommend imiquimod, podofilox, or sinecatechins as patient-administered options to treat genital and perianal warts, with no preference of one product over another
  - Treatment to remove genital warts should be guided by wart size, number, and anatomic site; cost; experience of the healthcare provider; adverse effects; and the preference of the patient
  - No definitive evidence suggests that any of the available treatments are superior to any other, and no single treatment is ideal for all patients or all warts

Dermatologics: Emollients

Magellan Medicaid Administration

Overview of Disease State – Emollients

- Atopic dermatitis (atopic eczema or eczema)
  - A common disease with worldwide prevalence
  - Clinically, eczematous patches and plaques are seen, which favor the face and extensor surfaces in young children and flexor surfaces (including the antecubital and popliteal fossae, ankles, and neck) in older children
  - Management of almost every case of atopic dermatitis will include topical therapy
    - Patients with mild to moderate eczema, topical therapy may be entirely sufficient to control disease activity
      - Emollients should be considered as first-line therapy for mild disease
    - Patients with more severe disease may require more advanced therapy including phototherapy or systemic therapy
      - Other topical therapeutic options for more advanced cases of atopic dermatitis include corticosteroids and calcineurin inhibitors

- Xerosis or dry skin
  - Caused by a loss of water in the upper layer of the skin
  - Emollients work by forming an oily layer on the top of the skin that traps water in the skin
  - These agents are designed to make the stratum corneum softer and more pliant by increasing its hydration
  - A large number of preparations are available, many of which are marketed as cosmetic and therapeutic moisturizers

Overview of Disease State – Emollients

- Place in Therapy
  - Emollients may be applied multiple times daily, and especially after bathing
  - Continued use of emollients during periods of disease quiescence can reduce the tendency for eczema flares
  - Studies have shown that moisturizers lessen symptoms and signs of atopic dermatitis, including pruritus, erythema, fissuring, and lichenification
  - Thus, resulting in some reduction in inflammation and atopic dermatitis dermatitis severity
  - In a study of 52 children with eczema treated with medium potency topical steroid to lesional skin for two weeks, subsequent daily application of emollient significantly improved xerosis and pruritus compared to no application of emollient
  - Patients are generally instructed to apply emollients liberally, though the clinical meaning of this term is subjective
  - A study of 67 pediatric patients (48 with eczema, 19 controls) found that 130 g/m^2/week of emollient was adequate for 95.8% of patients; however, the study did not detect differences in clinical response

Emollients – Indications & Dosing/Availability

- See Emollient TCR

Appendices

HIV Agents – Dosing and Availability

Drugs	Dosage in Adults	Dosage in Children	Special Dosing and Other Considerations	Availability
CCR5 Antagonist				
maraviroc (Selzentry), MVC	Concomitant use with potent CYP3A inhibitors including PIs (except tipranavir with ritonavir), delavirdine, elvitegravir/ritonavir, ketoconazole, itraconazole, clarithromycin, nefazodone: ▪ 150 mg twice daily Concomitant use with NRTIs, tipranavir with ritonavir, nevirapine, raltegravir, and other drugs that are not potent CYP3A inhibitors or CYP3A inducers: ▪ 300 mg twice daily Concomitant use with potent CYP3A inducers (e.g., efavirenz, etravirine, rifampin, carbamazepine, phenobarbital, phenytoin): ▪ 600 mg twice daily	Tablet If co-administered with a potent CYP3A inhibitor: Patient is ≥ 2 years of age: ▪ 10 kg to < 20 kg: 50 mg twice daily ▪ 20 kg to < 30 kg: 75 mg twice daily ▪ 30 kg to < 40 kg: 100 mg twice daily ▪ ≥ 40 kg: 150 mg twice daily If co-administered with tipranavir/ ritonavir, nevirapine, raltegravir, all NRTIs, and enfuvirtide: Patient is ≥ 2 years of age and ≥ 30 kg: ▪ 300 mg twice daily Oral solution If co-administered with a potent CYP3A inhibitor: Patient is 2 years of age and older: ▪ 10 kg to < 20 kg: 50 mg (2.5 mL) twice daily ▪ 20 kg to < 30 kg: 80 mg (4 mL) twice daily ▪ 30 kg to < 40 kg: 100 mg (5 mL) twice daily ▪ ≥ 40 kg: 150 mg (7.5ml) twice daily If co-administered with tipranavir/ ritonavir, nevirapine, raltegravir, all NRTIs, and enfuvirtide: Patient is ≥ 2 years of age and ≥ 30 kg: ▪ 300 mg (15 mL) twice daily It is not recommended to be coadministered with a potent CYP3A inducer	Renal impairment: Special dosing regimen for people with severe renal impairment or ESRD who are not receiving a concomitant CYP3A inhibitor or inducer and experience any symptoms of postural hypotension and therefore require a dose reduction (See Special Populations, Renal Impairment) Tropism testing with a highly sensitive tropism assay is required for the appropriate use of maraviroc	Tablets: 25 mg, 75 mg, 150 mg. 300 mg Oral Solution: 20 mg/mL

HIV Agents – Dosing and Availability

Drugs	Dosage in Adults	Dosage in Children	Special Dosing and Other Considerations	Availability
Fusion Inhibitor				
enfuvirtide (Fuzeon), T20 or ENF	90 mg (1 mL) twice daily injected subcutaneously (SC) into the upper arm, anterior thigh, or abdomen Do not inject near any anatomical areas where large nerves are close to the skin	Weight based Age 6 years to 16 years: ▪ 2 mg/kg twice daily up to a maximum dose of 90 mg twice daily injected SC Weight should be monitored periodically and dose adjustments made accordingly	Reconstitute with 1.1 mL of sterile water for injection Once reconstituted, this drug must be injected immediately or kept refrigerated in the original vial and used within 24 hours	90 mg single-use vials
Integrase Strand Transfer Inhibitors (INSTIs)				
dolutegravir (Tivicay), DTG	INSTI treatment-naïve: 50 mg once daily INSTI-experienced with certain INSTI-associated resistance substitutions or clinically suspected INSTI resistance: 50 mg twice daily Dolutegravir may be taken without regard to meals	Age ≥ 12 weighing ≥ 40 kg and INSTI treatment-naïve: 50 mg once daily Dolutegravir may be taken without regard to meals 30 kg to < 40 kg: 35 mg once daily Recommended weight based dose can be administered twice daily if certain UGT1A or CYP3A inducers are coadministered	Treatment naïve or INSTI-naïve co-administered with potent UGTIA/CYP3A inducers, efavirenz, fosamprenavir/ritonavir, tipranavir/ ritonavir, rifampin or carbamazepine: 50 mg twice daily	Film-coated tablet: 10 mg, 25 mg, 50 mg

HIV Agents – Dosing and Availability

Drugs	Dosage in Adults	Dosage in Children	Special Dosing and Other Considerations	Availability
Integrase Strand Transfer Inhibitors (INSTIs) (Continued)				
raltegravir (Isentress, Isentress HD)	400 mg twice daily with or without food HD: 1,200 mg (2 x 600 mg) once daily with or without food (in patients who are treatment-naïve or virologically suppressed on an initial regimen of 400 mg twice daily)	Weight/formulation-based; formulations are not bioequivalent Tablets or HD Tablets ▪ Children ≥ 40 kg and treatment-naïve or virologically suppressed on initial 400 mg twice daily regimen: 400 mg orally twice daily (Isentress) or 1,200 mg (2 x 600 mg; Isentress HD) once daily ▪ Children ≥ 25 kg: 400 mg twice daily (Isentress) Chewable Tablets ▪ ≥ 25 kg and ≤ 28 kg: 150 mg twice daily ▪ ≥ 28 kg and < 40 kg: 200 mg twice daily ▪ ≥ 40 kg: 300 mg twice daily ▪ Dosages for children weighing 11 to 25 kg: see dosing table in the package insert ▪ The 100 mg chewable tablet is scored and can be broken into equal halves Oral Suspension ▪ Dosage for 3 kg to 20 kg and ≥ 4 weeks of age is 2.5 mL to 10 mL (25 mg to 100 mg) twice daily based on weight; see labeling for additional details ▪ Dosage for birth to 4 weeks of age 2 kg to < 5 kg is 0.4 mL to 1.5 mL either once or twice daily (range, 4 mg to 30 mg/day); see labeling for additional details	During co-administration with rifampin, use 800 mg twice daily (2 x 400 mg) Film-coated and chewable tablets can be administered irrespective of food Suspension and Chewable tablets may not be substituted for the film-coated tablet as they are not bioequivalent Weight based and Pediatric dosing table available in prescribing information	Film-coated tablets: 400 mg (Isentress), 600 mg (Isentress HD) Chewable tablets (Isentress): 25 mg, 100 mg Granules for oral suspension (Isentress): 100 mg (single-use packets)

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HIV Agents – Dosing and Availability

Drugs	Dosage in Adults	Dosage in Children	Special Dosing and Other Considerations	Availability
Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)				
raltegravir (Isentress, Isentress HD)	400 mg twice daily with or without food HD: 1,200 mg (2 x 600 mg) once daily with or without food (in patients who are treatment-naïve or virologically suppressed on an initial regimen of 400 mg twice daily)	Weight/formulation-based; formulations are not bioequivalent Tablets or HD Tablets ▪ Children ≥ 40 kg and treatment-naïve or virologically suppressed on initial 400 mg	During co-administration with rifampin, use 800 mg twice daily (2 x 400 mg) Film-coated and chewable tablets can be administered irrespective of food Suspension and Chewable tablets may not be substituted for the film-coated tablet as they are not bioequivalent Weight based and Pediatric dosing table available in prescribing information	Film-coated tablets: 400 mg (Isentress), 600 mg (Isentress HD) Chewable tablets (Isentress): 25 mg, 100 mg Granules for oral suspension (Isentress): 100 mg (single-use packets)
delavirdine (Rescriptor), DLV	400 mg (four 100 mg or two 200 mg tablets) 3 times daily in combination with other antiretrovirals	--	Tablets may be dispersed in at least 3 ounces of water prior to consumption The 200 mg tablets should be taken as intact tablets because they are not readily dispersed in water	Tablets: 100 mg, 200 mg
doravirine (Pifeltro), DOR	100 mg once daily with or without food	--	Take daily at approximately the same time each day If administered with rifabutin; increase dose to 100 mg every 12 hours (twice daily) for duration of rifabutin use	Tablets: 100 mg
efavirenz (Sustiva), EFV	600 mg once daily (preferably at bedtime)	Weight based ≥ 3 months old and ≥ 3.5 kg: dosage varies from 100 mg to 400 mg daily for children 2.5 to < 40 kg, see dosing table in the package insert ≥ 40 kg: 600 mg daily	Advisable to be taken on an empty stomach at bedtime Capsules can be opened and administered by the sprinkle method for children who cannot swallow capsules or tablets	Capsules: 50 mg, 200 mg Tablets: 600 mg

HIV Agents – Dosing and Availability

Drugs	Dosage in Adults	Dosage in Children	Special Dosing and Other Considerations	Availability
Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs) (Continued)				
etravirine (Intelence), ETR	200 mg (one 200 mg tablet or two 100 mg tablets) taken twice daily following a meal	Weight based Age 2 years to < 18 years of age ▪ ≥ 10 kg to < 20 kg: 100 mg twice daily after meal ▪ ≥ 20 kg to < 25 kg: 125 mg twice daily after meal ▪ ≥ 25 kg to < 30 kg: 150 mg twice daily after meal ▪ ≥ 30 kg: 200 mg twice daily after meal	Pregnant patients: ▪ 200 mg twice daily following a meal Patients who are unable to swallow tablets whole may disperse them in a glass of water; once dispersed, the dispersion should be stirred well and immediately consumed; the glass should be rinsed with liquid several times and each rinse completely swallowed to ensure the entire dose is consumed (once dispersed in a small amount of water, it may be further diluted in milk or orange juice to improve taste; warm or carbonated beverages should be avoided)	Tablets: 25 mg, 100 mg, 200 mg
nevirapine (Viramune), NVP	200 mg tablet daily for the first 14 days, followed by one 200 mg tablet twice daily, in combination with other antiretrovirals	Body Surface Area (BSA) based 15 days of age and older: ▪ 150 mg/m2 once daily for 14 days, followed by 150 mg/m2 twice daily thereafter Total daily dose should not exceed 400 mg for any patient	An additional 200 mg dose following each dialysis treatment should be administered Dose escalation during the lead-in period should not be pursued if a rash occurs and has not yet resolved The maximum lead-in dosing period should not exceed 28 days	Tablets: 200 mg Suspension, oral: 50 mg/5 mL (as nevirapine hemihydrate)
nevirapine extended-release (Viramune XR)	Initiate 200 mg immediate-release tablet daily for first 14 days followed by 400 mg extended-release tablet daily. If patient has been stabilized on nevirapine immediate-release tablets twice daily, then no lead-in period is needed	BSA based (must be ≥ 1.17m2) 6 years to < 18 years of age: ▪ Initiate as 150 mg/m2 once daily using immediate release tablets or oral suspension for 14 days (not to exceed 200 mg daily), then 400 mg XR tablet once daily Total daily dose should not exceed 400 mg for any patient	Initiation of treatment is not recommended in the following patient types: adult females with CD4 counts of 250 cells per mm3 and adult males with CD4 counts of 400 cells per mm3 If dosing is interrupted for more than 7 days, the 14-day lead-in period must be re-initiated	Extended-release tablets: 100 mg (generic only), 400 mg
rilpivirine (Edurant), RPV	25 mg tablet once daily with a meal	Weight based Treatment-naïve ≥ 12 years old: ▪ ≥ 35 kg: 25 mg once daily with a meal	When co-administering with rifabutin, the dose should be increased to 50 mg (2 tablets of 25 mg each) once daily with a meal; if rifabutin is discontinued, the Edurant dose should be decreased to 25 mg once daily with a meal	Tablets: 25 mg

HIV Agents – Dosing and Availability

Drugs	Dosage in Adults	Dosage in Children	Special Dosing and Other Considerations	Availability
Nucleoside Reverse Transcriptase Inhibitors (NRTIs)				
abacavir (Ziagen), ABC	300 mg twice daily or 600 mg once daily with other antiretrovirals	Weight based Tablets: ▪ 14 kg to 21 kg: 150 mg twice daily ▪ 21 kg to < 30 kg: 150 mg in morning and 300 mg in evening ▪ ≥ 30 kg: 300 mg twice daily Oral Solution, ≥ 3 months of age: ▪ 8 mg/kg twice daily or 16 mg/kg once daily; Not to exceed a maximum dose of 600 mg daily	May be taken irrespective of food Tablets may be used in pediatric patients able to reliably swallow tablets	Tablets: 300 mg Solution, oral: 20 mg/mL
didanosine (Videx Solution), ddI	Preferred Dosing: ▪ At least 60 kg: 200 mg twice daily ▪ < 60 kg: 125 mg twice daily Dosing for patients requiring once daily therapy: ▪ At least 60 kg: 400 mg once daily ▪ < 60 kg: 250 mg once daily	Age and BSA based ▪ 2 weeks to 8 months old: 100 mg/m2 twice daily ▪ ≥ 8 months old: 120 mg/m2 twice daily Do not exceed the adult dosing recommendation	Special dosing regimen for people with CrCl < 60 mL/min (See Special Populations, Renal Impairment) Administer on an empty stomach at least 30 minutes before or 2 hours after eating	Pediatric powder for oral solution: 10 mg/mL (brand only)
didanosine EC (Videx EC), ddI	Weight based ▪ 20 kg to less than 25 kg: 200 mg once daily ▪ 25 kg to less than 60 kg: 250 mg once daily ▪ ≥ 60 kg: 400 mg once daily	Same dosing for pediatric and adult patients Consider the Pediatric Powder for Oral Solution for pediatric patients weighing < 20 kg or who cannot swallow capsules	Special dosing regimen for people with CrCl < 60 mL/min (See Special Populations, Renal Impairment) Patients who weigh < 60 kg should use an alternate didanosine formulation	Capsules: 125 mg, 200 mg, 250 mg, 400 mg

HIV Agents – Dosing and Availability

Drugs	Dosage in Adults	Dosage in Children	Special Dosing and Other Considerations	Availability
Nucleoside Reverse Transcriptase Inhibitors (NRTIs) (Continued)				
emtricitabine (Emtriva), FTC	200 mg once daily	Weight based ▪ 3 months to 17 years (weight ≥ 33 kg, able to swallow an intact capsule): 200 mg capsule administered once daily orally	Special dosing regimen for people with CrCl 50 mL/min or less (See Special Populations, Renal Impairment); If given on hemodialysis days, give after chemotherapy	Capsules: 200 mg
emtricitabine solution (Emtriva)	240 mg (24 mL) administered once daily orally	Age/Weight based ▪ 0 to 3 months: 3 mg/kg, administered once daily orally ▪ 3 months to 17 years: 6 mg/kg up to a maximum of 240 mg (24 mL), administered once daily orally	Special dosing regimen for people with ≤ CrCl 50 mL/min or less (See Special Populations, Renal Impairment); If given on hemodialysis days, give after hemodialysis	Solution, oral: 10 mg/mL
lamivudine (Epivir), 3TC	Adults and adolescents over 16 years of age: ▪ 300 mg once daily or 150 mg twice daily	Weight based Age 3 months to 16 years of age Oral Solution ▪ 4 mg/kg twice daily or 8 mg/kg once daily, not to exceed 300 mg daily Tablets ▪ 14 kg to < 20 kg: 75 mg twice daily ▪ ≥ 20 kg to < 25 kg: 75 mg in morning and 150 mg in the evening ▪ ≥ 25 kg: 150 mg twice daily	--	Tablets: 150 mg, 300 mg Solution, oral: 10 mg/mL
stavudine (Zerit), d4t	Weight-based ▪ < 60 kg: ▪ 30 mg every 12 hours ▪ ≥ 60 kg: 40 mg every 12 hours	Age based ▪ Newborns from birth to 13 days old 0.5 mg/kg every 12 hours ▪ 14 days and older and weighing < 30 kg: 1 mg/kg every 12 hours ▪ ≥ 30 kg: Refer to adult dosing	Solution requires reconstitution by a pharmacist and should be refrigerated and discarded after 30 days	Capsules: 15 mg (generic only), 20 mg, 30 mg, 40 mg Solution, oral: 1 mg/mL (brand only)

HIV Agents – Dosing and Availability

Drugs	Dosage in Adults	Dosage in Children	Special Dosing and Other Considerations	Availability
Nucleoside Reverse Transcriptase Inhibitors (NRTIs) (Continued)				
zidovudine (Retrovir), AZT	600 mg daily in divided doses with other antiretroviral agents	Weight based Ages 4 weeks to < 18 years ▪ 4 kg to < 9 kg: 24 mg/kg daily, in 2to 3 divided doses ▪ 9 kg to < 30 kg: 18 mg/kg daily, in 2 to 3 divided doses ▪ ≥ 30 kg: 600 mg daily, in 2 to 3 divided doses Birth to 6 weeks of age ▪ Oral: 2 mg/kg every 6 hours ▪ IV: 1.5 mg/kg (infused over 30 minutes) every 6 hours	Prevention of maternal-fetal HIV-1 transmission: ▪ Maternal Dosing: 100 mg orally 5 times per day until the start of labor ▪ Neonatal Dosing: Start neonatal dosing within 12 hours after birth and continue through 6 weeks of age Pediatric dosing can be based on body surface area: 480 mg/m2/day in 2 to 3 divided doses The vial stopper on the injection contains dry natural rubber, which may cause allergic reactions in latex-sensitive patients An oral syringe with 0.1 mL graduation is recommended for neonates	Capsules: 100 mg Syrup, oral: 50 mg/5 mL Tablets: 300 mg (generic only)
Nucleotide Reverse Transcriptase Inhibitor (NRTI)				
tenofovir disoproxil fumarate (Viread), TDF	300 mg once daily	Age/Weight based Adults and pediatric patients ▪ ≥ 35 kg: 300 mg once daily ≥ 2 years, weight ≥ 17 kg, able to swallow an intact tablet ▪ 17 kg to < 22 kg: 150 mg once daily ▪ 22 kg to < 28 kg: 200 mg once daily ▪ 28 kg to < 35 kg: 250 mg once daily ▪ ≥ 35 kg: 300 mg once daily	Oral powder available for pediatric patients ≥ 2 years old with a body weight ≥ 10 kg and unable to swallow a tablet. Dosage is approximately 8 mg/kg once daily (maximum 300 mg); see product label for detailed dosing. Special dosing regimen for people with CrCl < 50 mL/min (See Special Populations, Renal Impairment) May be taken irrespective of food	Tablet: 150 mg (brand only), 200 mg (brand only), 250 mg (brand only), 300 mg Oral powder: 40 mg/scoop (gram) (brand only)

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HIV Agents – Dosing and Availability

Drugs	Dosage in Adults	Dosage in Children	Special Dosing and Other Considerations	Availability
Pharmacokinetic Enhancer				
cobicistat (Tybost), COBI or c	Concomitant use with atazanavir or darunavir: ▪ 150 mg once daily with food	--	Not interchangeable with ritonavir to increase systemic exposure of darunavir 600 mg twice daily, fosamprenavir, saquinavir, or tipranavir Not recommended with darunavir 600 mg twice daily, fosamprenavir, saquinavir, or tipranavir	Tablets: 150 mg
Protease Inhibitors (PIs)				
atazanavir (Reyataz), ATV	Treatment-naïve patients: ▪ 300 mg with ritonavir 100 mg once daily with food ▪ When co-administered with tenofovir disoproxil fumarate, H2-receptor antagonist, or a proton pump inhibitor: ▪ 300 mg with ritonavir 100 mg once daily with food ▪ When coadministered with efavirenz: 400 mg with ritonavir 100 mg once daily with food ▪ If unable to tolerate ritonavir: 400 mg once daily with food	Weight based Capsules- Pediatric patients (6 years to < 18 years of age): ▪ 15 kg to < 35 kg: 200 mg with ritonavir 100 mg once daily with food ▪ At least 35 kg: 300 mg with ritonavir 100 mg once daily with food Capsules- Pediatric patients unable to tolerate ritonavir (treatment-naïve, ≥ 13 years of age, ≥ 40 kg): ▪ 400 mg once daily with food Oral Powder- Treatment-naïve or experienced pediatric patients (≥ 3 months old and weigh 5 kg to < 25 kg: ▪ 5 kg to < 15 kg: 200 mg mixed with food or drink; followed immediately with ritonavir 80 mg; once daily (Treatment naïve to PI, pediatric patients 5 kg to < 10 kg who may not tolerate 200 mg, may decrease dose to 150 mg with close HIV viral load monitoring)	Renal impairment: ▪ Treatment-naïve patients with end-stage renal disease (ESRD) managed with hemodialysis: atazanavir 300 mg with ritonavir 100 mg ▪ Treatment-experienced patients with ESRD managed with hemodialysis: Should not be administered Hepatic impairment: Special dosing regimen may be necessary (See Special Populations, Hepatic Impairment) Concomitant therapy: Dosing modifications for some concomitant medications required (e.g., H2-receptor antagonists and tenofovir disoproxil fumarate) Oral powder must be taken with concomitant ritonavir oral solution Oral powder contains phenylalanine; avoid or use with caution in patients with phenylketonuria	Capsules: 150 mg, 200 mg, 300 mg Oral powder for suspension: 50 mg packet

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HIV Agents – Dosing and Availability

Drugs	Dosage in Adults	Dosage in Children	Special Dosing and Other Considerations	Availability
Protease Inhibitors (PIs)				
atazanavir (Reyataz), ATV, (continued)	Treatment-experienced patients: ▪ 300 mg with ritonavir 100 mg once daily with food Pregnancy: ▪ 300 mg with ritonavir 100 mg once daily with food ▪ Should not be administered without ritonavir ▪ When co-administered with tenofovir or an H2-receptor antagonist in 2nd or 3rd trimester: 400 mg with ritonavir 100 mg once daily with food	▪ 15 kg to < 25 kg: 250 mg mixed with food or drink; followed immediately with ritonavir 80 mg; once daily ▪ At least 25 kg, but who cannot swallow the capsule: 300 mg mixed with food or drink; followed immediately with ritonavir 100 mg; once daily Dosage based on body weight should not exceed the adult dose Doses must be taken with food		

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HIV Agents – Dosing and Availability

Drugs	Dosage in Adults	Dosage in Children	Special Dosing and Other Considerations	Availability
Protease Inhibitors (PIs) (Continued)				
darunavir (Prezista), DRV	Testing is recommended in treatment-experienced patients to assess virus susceptibility to darunavir Treatment-naïve and treatment-experienced adult patients with no darunavir resistance associated substitutions: ▪ 800 mg (one 800 mg tablet) with ritonavir 100 mg once daily with food Treatment-experienced adult patients with at least 1 darunavir resistance associated substitution: ▪ 600 mg (one 600 mg tablet) with ritonavir 100 mg twice daily with food	Weight based Treatment-naïve or Treatment-experienced with no darunavir resistance associated substitutions (ages 3 years to < 18 years and weighing ≥ 10 kg) ▪ 10 kg to < 11 kg: 350 mg with 64 mg ritonavir once daily with food ▪ 11 kg to < 12 kg: 385 mg with 64 mg ritonavir once daily with food ▪ 12 kg to < 13 kg: 420 mg with 80 mg ritonavir once daily with food ▪ 13 kg to < 14 kg: 455 mg with 80 mg ritonavir once daily with food ▪ 14 kg to < 15 kg: 490 mg with 96 mg ritonavir once daily with food ▪ 15 kg to < 30 kg: 600 mg with 100 mg ritonavir once daily with food ▪ 30 kg to < 40 kg: 675 mg with 100 mg ritonavir once daily with food ▪ ≥ 40 kg: 800 mg with 100 mg ritonavir once daily with food Do not exceed the treatment-experienced adult dose	Hepatic Insufficiency: special dosing regimen for people hepatic impairment may be required; not recommended in severe hepatic impairment (See Special Populations, Hepatic Impairment) Pediatric dosing for patients weighing between 10 kg and 15 kg is with the oral suspension; pediatric patients weighing at least 15 kg can be dosed with oral tablets or oral suspension if able to swallow tablets reliably Pregnant patients: ▪ 600 mg with ritonavir 100 mg twice daily with food ▪ In those who are already stable and virologically suppressed (HIV-1 RNA < 50 copies/mL) on 800 mg with 100 mg ritonavir daily should remain at that dose	Tablets:75 mg, 150 mg, 600 mg, 800 mg Oral suspension: 100 mg/mL

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HIV Agents – Dosing and Availability

Drugs	Dosage in Adults	Dosage in Children	Special Dosing and Other Considerations	Availability
Protease Inhibitors (PIs) (Continued)				
darunavir (Prezista), DRV, (continued)		Treatment-experienced with ≥ 1 darunavir resistance associated substitutions (ages 3 years to < 18 years and weighing ≥ 10 kg) ▪ 10 kg to < 11 kg: 200 mg with 32 mg ritonavir twice daily with food ▪ 11 kg to < 12 kg: 220 mg with 32 mg ritonavir twice daily ▪ 12 kg to < 13 kg: 240 mg with 40 mg ritonavir twice daily with food ▪ 13 kg to < 14 kg: 260 mg with 40 mg ritonavir twice daily with food ▪ 14 kg to < 15 kg: 280 mg with 48 mg ritonavir twice daily with food ▪ 15 kg to < 30 kg: 375 mg with 48 mg ritonavir twice daily with food ▪ 30 kg to < 40 kg: 450 mg with 60 mg ritonavir twice daily with food ▪ ≥ 40 kg: 600 mg with 100 mg ritonavir twice daily		

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HIV Agents – Dosing and Availability

Drugs	Dosage in Adults	Dosage in Children	Special Dosing and Other Considerations	Availability
Protease Inhibitors (PIs) (Continued)				
fosamprenavir (Lexiva), FPV	Therapy-Naïve Adults: ▪ 1,400 mg twice daily ▪ 1,400 mg once daily plus ritonavir 200 mg once daily ▪ 1,400 mg once daily plus ritonavir 100 mg once daily ▪ 700 mg twice daily plus ritonavir 100 mg twice daily PI-Experienced Adults: ▪ 700 mg twice daily plus ritonavir 100 mg twice daily	Weight based PI-naïve, 28 days post-natal and older, and protease inhibitor-experienced 6 months of age and older: ▪ < 11 kg: 45 mg/kg plus ritonavir 7 mg/kg ▪ 11 kg to < 15 kg: 30 mg/kg plus ritonavir 3 mg/kg ▪ 15 kg to < 20 kg: 23 mg/kg plus ritonavir 3 mg/kg ▪ ≥ 20 kg: 18 mg/kg plus ritonavir 3 mg/kg When dosing with ritonavir, do not exceed the adult dose of fosamprenavir 700 mg/ritonavir 100 mg twice daily dose. PI-naïve, 2 years of age and older: ▪ 30 mg/kg without ritonavir Do not exceed adult daily dose	Hepatic Impairment: Special dosing regimen for people hepatic impairment may be required (See Special Populations, Hepatic Impairment) Adults should take the suspension without food, but pediatric patients should take the suspension with food; tablets may be taken with or without food	Tablets: 700 mg Suspension, oral: 50 mg/mL (brand only)
indinavir (Crixivan), IDV	800 mg (usually two 400 mg capsules) every 8 hours Ensure adequate hydration by drinking at least 1.5 liters (approximately 48 ounces) of liquids during the course of 24 hours Administer without food but with water 1 hour before or 2 hours after a meal.	--	Concomitant Drugs: ▪ Delavirdine 400 mg 3 times daily: indinavir 600 mg every 8 hours ▪ Didanosine: separate by 1 hour from indinavir dosing ▪ Itraconazole 200 mg twice daily: indinavir 600 mg every 8 hours ▪ Ketoconazole: indinavir 600 mg every 8 hours ▪ Rifabutin: increase dose to indinavir 1000 mg every 8 hours; dose reduction of rifabutin required Hepatic Insufficiency: special dosing regimen for people hepatic impairment may be required (See Special Populations, Hepatic Impairment)	Capsules: 200 mg, 400 mg

HIV Agents – Dosing and Availability

Drugs	Dosage in Adults	Dosage in Children	Special Dosing and Other Considerations	Availability
Protease Inhibitors (PIs) (Continued)				
nelfinavir (Viracept), NFV	▪ 1,250 mg (five 250 mg tablets or two 625 mg tablets) twice daily, or ▪ 750 mg (three 250 mg tablets) 3 times daily with meals Patients unable to swallow the 250 or 625 mg tablets may dissolve the tablets in a small amount of water; once dissolved, patients should mix the cloudy liquid well, and consume it immediately; the glass should be rinsed with water and the rinse swallowed to ensure the entire dose is consumed	Weight based Ages ≥ 2 years of age Dosing for children using 250 mg tablets: ▪ 10 kg to 12 kg: 2 tablets twice daily or 1 tablet 3 times daily ▪ 13 kg to 18 kg: 3 tablets twice daily or 2 tablets 3 times daily ▪ 19 kg to 20 kg: 4 tablets twice daily or 2 tablets 3 times daily ▪ ≥ 21 kg: 4 to 5 tablets twice daily or 3 tablets 3 times daily, maximum dose ▪ Max Dose: 2,500 mg daily Dosing for children using oral powder for solution: ▪ 9 kg to < 10.5 kg: 10 scoops twice daily or 6 scoops 3 times daily ▪ 10.5 kg to < 12 kg: 11 scoops twice daily or 7 scoops 3 times daily ▪ 12 kg to < 14 kg: 13 scoops twice daily or 8 scoops 3 times daily ▪ 14 kg to < 16 kg: 15 scoops twice daily or 9 scoops 3 times daily ▪ 16 to <18 kg: 10 scoops 3 times daily ▪ 18 to <23 kg: 12 scoops 3 times daily ▪ ≥23 kg: 15 scoops 3 times daily ▪ Max dose: 2,500 mg daily	Oral Powder for Solution may be an option for children who are unable to swallow tablets; the oral powder may be mixed with a small amount of water, milk, formula, soy formula, soy milk, or dietary supplements; once mixed, the entire contents must be consumed in order to obtain the full dose; if the mixture is not consumed immediately, it must be refrigerated, but storage must not exceed 6 hours Acidic food or juice is not recommended for concomitant use because the combination may result in a bitter taste The oral powder should not be reconstituted with water in its original container Pediatric dosing with oral powder based on 45 to 55 mg/kg twice daily or 25 to 35 mg/kg 3 times daily with meals; all doses should be given with meals	Tablets: 250 mg, 625 mg

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HIV Agents – Dosing and Availability

Drugs	Dosage in Adults	Dosage in Children	Special Dosing and Other Considerations	Availability
Protease Inhibitors (PIs) (Continued)				
tipranavir (Aptivus), TPV	500 mg (two 250 mg capsules or 5 mL of oral solution) twice daily in combination with ritonavir 200 mg	Weight or Body Surface Area based Ages 2 to 18 years ▪ 14 mg/kg with 6 mg/kg of ritonavir twice daily, or ▪ 375 mg/m2 with ritonavir 150 mg/m2 Decreased dosing due to intolerance or toxicity: ▪ 12 mg/kg with 5 mg/kg of ritonavir twice daily, or ▪ 290 mg/m2 with ritonavir 115 mg/m2 Assess ability to swallow capsules prior to initiating therapy; if a child is unable to reliably swallow a capsule, then the oral solution formulation should be used; do not exceed adult dose	Capsules require refrigeration and should be swallowed whole; once the bottle is opened, the contents must be used within 60 days; the bottle may be removed from refrigeration briefly so long as the bottle remains at room temperature; write the date of opening the bottle on the label and do not use after that date Oral solution must be maintained at room temperature and used within 60 days after first opening of the bottle Can be taken irrespective of food	Capsules: 250 mg Solution, oral: 100 mg/mL
Recombinant Monoclonal Antibody				
ibalizumab-uiyk (Trogarzo)	Loading dose: 2,000 mg as an intravenous (IV) infusion Maintenance dosage: 800 mg IV infusion every 2 weeks	--	Requires further dilution in 0.9% NaCl; see labeling for preparation details Patients must be observed for 1 hour after completion of administration for at least the first infusion; if no infusion-associated adverse reaction occurs, the post-infusion observation time can be reduced to 15 minutes thereafter Dose modifications are not required with any other drugs	Single-dose vials of IV solution: 200 mg/1.33 mL

HIV Agents – Dosing and Availability

Drugs	Dosage in Adults	Dosage in Children	Special Dosing and Other Considerations	Availability
Combination Products – Nucleos(t)ide Reverse Transcriptase Inhibitors (NRTIs)				
abacavir/ lamivudine (Epzicom), ABC/3TC	1 tablet daily, in combination with other antiretroviral agents	≥ 25 kg who are able to swallow: 1 tablet daily, in combination with other antiretroviral agents	Do not use for patients requiring dosage adjustment such as those with creatinine clearance < 50 mL/min and patients with hepatic impairment Can be taken irrespective of food	Tablets: 600/300 mg abacavir/ lamivudine
abacavir/ lamivudine/ zidovudine (Trizivir), ABC/3TC/AZT	1 tablet twice daily	Not recommended for use in adolescents who weigh < 40 kg	Do not use for patients requiring dosage adjustment such as those with creatinine clearance < 50 mL/min, patients with hepatic impairment, or patients experiencing dose-limiting adverse events Can be taken irrespective of food	Tablets: 150/300/300 mg lamivudine/ abacavir/ zidovudine
tenofovir alafenamide/ emtricitabine (Descovy), TAF/FTC	Treatment of HIV-1 in combination with other antiretrovirals: ▪ 200/25 mg (1 regular strength tablet) once daily without regards to meals	In combination with antiviral agents (other than protease inhibitors that require CYP3A inhibitors) for HIV-1 in pediatric patients weighing ≥ 25 kg to < 35 kg ▪ 200/25 mg (1 regular strength tablet) once daily without regards to meals Safety and efficacy co-administered with a PI and either cobicistat or ritonavir have not been established in patients < 35 kg	Not indicated for people with CrCl ≤ 30 mL/min (See Special Populations, Renal Impairment)	Tablets: 200/25 mg emtricitabine/ tenofovir alafenamide
lamivudine/ tenofovir disoproxil fumarate (Cimduo)	1 tablet once daily	Pediatric patients weighing ≥ 35 kg: 1 tablet once daily	Not recommended in patients with estimated CrCl < 50 mL/min, ESRD, or hemodialysis	Tablets: 300/300 mg lamivudine/ tenofovir disoproxil fumarate

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HIV Agents – Dosing and Availability

Drugs	Dosage in Adults	Dosage in Children	Special Dosing and Other Considerations	Availability
Combination Products – Nucleos(t)ide Reverse Transcriptase Inhibitors (NRTIs) (continued)				
lamivudine/ zidovudine (Combivir), AZT/3TC/AZT	Adults and Adolescents weighing ≥ 30 kg: 1 tablet twice daily	Pediatric patients must weigh ≥ 30 kg; do not exceed adult doses	Fixed dose zidovudine/lamivudine products should not be used for pediatric patients weighing < 30 kg or patients requiring dosage adjustment, such as those with renal (CrCl < 50 mL/min) or hepatic impairment, or patients experiencing dose-limiting adverse reactions	Tablets, scored: 150/300 mg lamivudine/ zidovudine
tenofovir disoproxil fumarate/ emtricitabine (Truvada), TDF/FTC	Treatment of HIV-1: ▪ 200/300 mg (1 regular strength tablet) once daily Pre-exposure Prophylaxis (PrEP): ▪ 200/300 mg (1 regular strength tablet) once daily	Treatment of HIV-1 weighing ≥ 35 kg: ▪ 200/300 mg (1 regular strength tablet) once daily Treatment of HIV-1 weighing 17 kg to < 35 kg and able to swallow a whole tablet (using lower-strength tablets): ▪ 17 to < 22 kg: 100/150 mg tablet once daily ▪ 22 to < 28 kg: 133/200 mg tablet once daily ▪ 28 to < 35 kg: 167/250 mg tablet once daily Pre-exposure Prophylaxis (PrEP) weighing ≥ 35 kg: ▪ 200/300 mg (1 regular strength tablet) once daily	Special dosing regimen for people with CrCl < 50 mL/min (See Special Populations, Renal Impairment) Not to be used in non-HIV-1 infected individuals for PrEP with a creatinine clearance < 60 mL/min Can be taken irrespective of food	Tablets: 100/150 mg, 133/200 mg, 167/250 mg, 200/300 mg (regular strength) emtricitabine/ tenofovir disoproxil fumarate
Combination Products – Protease Inhibitors (PIs) or PIs + Pharmacokinetic Enhancer				
atazanavir/ cobicistat (Evotaz), ATV/c	1 tablet orally once daily with food	--	Not recommended for use in treatment-experienced patients with end-stage renal disease managed with hemodialysis Not recommended in patients with hepatic impairment	Tablets: 300/150 mg atazanavir/ cobicistat

Magellan Rx MANAGEMENT℠

HIV Agents – Dosing and Availability

Drugs	Dosage in Adults	Dosage in Children	Special Dosing and Other Considerations	Availability
Combination Products – Protease Inhibitors (PIs) or PIs + Pharmacokinetic Enhancer (Continued)				
darunavir/ cobicistat (Prezcobix), DRV/c	1 tablet orally once daily with food	--	--	Tablets: 800/150 mg darunavir/ cobicistat
lopinavir/ ritonavir (Kaletra), LPVr	400/100 mg (two 200/50 mg tablets, four 100/25 mg capsules, or 5 mL oral solution) twice daily Patients with less than 3 lopinavir resistance-associated substitutions: ▪ 800/200 mg (four 200/50 mg tablets or 10 mL oral solution) once daily Concomitant therapy with efavirenz, nevirapine, or nelfinavir: ▪ 500/125 mg (two 200/50 mg tablets and one 100/25 mg tablet) twice daily ▪ 533/133 mg (6.5 mL) twice daily Pregnant woman ▪ 400/100 mg twice daily	Weight or Body Surface Area based ▪ Pediatric patients < 12 years of age with a weight > 40 kg OR age > 12 years of age: 400/100 mg (three 133/33 mg capsules) twice daily with food Pediatric patients between 14 days to 6 months of age, oral solution: ▪ 16/4 mg/kg twice daily, OR ▪ 300/75 mg/m2 twice daily Pediatric patients between 6 months and 18 years of age, oral solution: ▪ 230/57.5 mg/m2 twice daily; not to exceed adult dose of 400/100 mg twice daily, OR ▪ < 15 kg: 12/3 mg/kg twice daily ▪ ≥ 15 kg to 40 kg: 10/2.5 mg/kg twice daily Concomitant therapy with efavirenz, nevirapine, or nelfinavir: ▪ > 45 kg, capsules: 533/133 mg (four 133/33 mg capsules) twice daily with food ▪ 6 months to 18 years of age, oral solution: 300/75 mg/m2 oral solution ▪ < 15 kg, oral solution: 13/3.25 mg/kg twice daily ▪ > 15 kg to 45 kg, oral solution: 11/2.75 mg/kg twice daily	Do not use once daily administration of Kaletra in HIV-1 infected patients with 3 or more lopinavir resistance-associated substitutions; concomitant carbamazepine, phenobarbital, or phenytoin; or in combination with efavirenz, nevirapine, or nelfinavir Tablets may be taken with or without food, swallowed whole and not chewed, broken, or crushed Oral solution must be taken with food Once daily dosing is not approved in pediatric patients less than 18 years of age Dose increase is required for pediatric patients taking concomitant efavirenz, nevirapine, or nelfinavir; use not recommended in patients taking these agents who are < 6 months of age Kaletra oral solution should not be administered to neonates before a postmenstrual age (first day of the mother's last menstrual period to birth plus the time elapsed after birth) of 42 weeks and a postnatal age of at least 14 days has been attained or to pregnant woman	Solution, oral: 80/20 mg per mL lopinavir/ritonavir Tablet, film coated: 100/25 mg, 200/50 mg lopinavir/ritonavir (brand only)

HIV Agents – Dosing and Availability

Drugs	Dosage in Adults	Dosage in Children	Special Dosing and Other Considerations	Availability
Combination Products – Multiple Classes				
bictegravir/ emtricitabine/ tenofovir alafenamide (Biktarvy), BIC/FTC/TAF	1 tablet orally once daily with or without food	--	Not recommended in patients with CrCl < 30 mL/min Not recommended in patients in patients with Child-Pugh Class C	Tablets: 50/200/25 mg bictegravir/ emtricitabine/ tenofovir alafenamide
darunavir/ cobicistat/ emtricitabine/ tenofovir alafenamide (Symtuza), DRV/c/FTC/TAF	1 tablet orally once daily with food	--	Not recommended in patients with CrCl < 30 mL/min Not recommended in patients in patients with Child-Pugh Class C	Tablets: 800/150/200/10 mg darunavir/cobicistat/ emtricitabine/ tenofovir alafenamide
dolutegravir/ abacavir/ lamivudine (Triumeq), DTG/ABC/3TC	1 tablet once daily with or without food	Pediatric patients weighing ≥ 40 kg: 1 tablet once daily with or without food	If co-administered with efavirenz, fosamprenavir/ritonavir, tipranavir/ ritonavir, rifampin or carbamazepine, recommend dolutegravir dosage of 50 mg twice daily; an additional dolutegravir 50 mg tablet, separated by 12 hours from Triumeq, should be taken	Tablets: 600/50/300 mg abacavir/dolutegravir/ lamivudine
dolutegravir/rilpivirine (Juluca), DTG/RPV	1 tablet once daily with food	--	Coadministration with rifabutin: 1 tablet (dolutegravir 50 mg/rilpivirine 25 mg) plus 1 rilpivirine 25 mg tablet orally once daily with a meal during the rifabutin regimen	Tablets: 50/25 mg dolutegravir/rilpivirine
doravirine/ lamivudine/tenofovir disoproxil fumarate (Delstrigo), DOR/3TC/TDF	1 tablet once daily with or without food	--	--	Tablet: 100/300/300 mg doravirine/lamivudine/ tenofovir disoproxil fumarate
efavirenz/lamivudine/ tenofovir disoproxil fumarate (Symfi, Symfi Lo), EFV/3TC/TDF	Symfi, Symfi Lo: 1 tablet taken orally once daily on an empty stomach, preferably at bedtime	Symfi Lo Pediatric patients weighing ≥ 35 kg: ▪ 1 tablet taken orally once daily on an empty stomach, preferably at bedtime Symfi Pediatric patients weighing ≥ 40 kg: ▪ 1 tablet taken orally once daily on an empty stomach, preferably at bedtime	---	Symfi – Tablets: 600/300/300 mg efavirenz/lamivudine/ tenofovir disoproxil fumarate Symfi Lo – Tablets: 400/300/300 mg efavirenz/lamivudine/ tenofovir disoproxil fumarate

HIV Agents – Dosing and Availability

Drugs	Dosage in Adults	Dosage in Children	Special Dosing and Other Considerations	Availability
Combination Products – Multiple Classes (Continued)				
elvitegravir/cobicistat/ emtricitabine/ tenofovir alafenamide (TAF) (Genvoya), EVG/c/FTC/TAF	1 tablet once daily with food	Pediatric patients weighing ≥ 25 kg: 1 tablet once daily with food	Not recommended in patients with estimated CrCl 15 to < 30 mL/min or with CrCl < 15 mL/min in patients not on chronic hemodialysis Not recommended in patients with severe hepatic impairment	Tablets: 150/150/200/10 mg elvitegravir/cobicistat/ emtricitabine/ tenofovir alafenamide
elvitegravir/cobicistat/ emtricitabine/ tenofovir disoproxil fumarate (Stribild), EVG/c/FTC/TDF	1 tablet once daily with food	Pediatric patients ≥ 12 years old and weighing ≥ 35 kg: 1 tablet once daily with food	Should not be initiated in patients with estimated creatinine clearance below 70 mL per minute; discontinue in patients with estimated CrCl < 50 mL/min or evidence of Fanconi syndrome. Should be taken with food Because it is considered a complete regimen, it should not be coadministered with other antiretroviral products	Tablets: 150/150/200/300 mg elvitegravir/cobicistat/ emtricitabine/ tenofovir disoproxil fumarate
emtricitabine/ rilpivirine/tenofovir alafenamide (Odefsey), FTC/RPV/TAF	1 tablet once daily with a meal	Age ≥ 12 years: 1 tablet once daily with a meal	Not recommended in patients with estimated CrCl < 30 mL/min Not studied in patients with severe hepatic impairment	Tablets: 200/25/25 mg emtricitabine/ rilpivirine/tenofovir alafenamide
rilpivirine/ emtricitabine/ tenofovir disoproxil fumarate (Complera), RPV/FTC/TDF	1 tablet once daily with a meal If co-administered with rifabutin, an additional 25 mg tablet of rilpivirine (Edurant) once per day is recommended	Age ≥ 12 years weighing ≥ 35 kg: 1 tablet once daily with a meal	Should not be administered in patients with creatinine clearance < 50 mL/min For pregnant patients: ▪ If patients are already taking Complera and virologically suppressed (HIV-RNA < 50 copies/mL), Complera 1 tablet taken once daily may be continued	Tablets: 25/200/300 mg rilpivirine/ emtricitabine/ tenofovir disoproxil fumarate
tenofovir disoproxil fumarate/ emtricitabine/ efavirenz (Atripla), TDF/FTC/EFV	1 tablet once daily on an empty stomach, preferably at bedtime	≥ 40 kg: 1 tablet once daily on an empty stomach, preferably at bedtime	Should not be administered in patients with creatinine clearance < 50 mL/min Co-administration with rifampin requires dose modification of the efavirenz component Dosage adjustment with rifampin coadministration: additional 200 mg/day of efavirenz is recommended for patients weighing ≥ 50 kg	Tablets: 600/200/300 mg efavirenz/ emtricitabine/ tenofovir disoproxil fumarate