ARIZONA HEALTH CARE COST CONTAINMENT SYSTEM

AHCCCS Pharmacy and Therapeutics Committee

May 19, 2026

SMART Therapy

Dr. Christina Kwong and Dr. Roy Jedeikin

SMART for Asthma:
Preventing Exacerbations, Preventing Harm

Rationale for a Standardized Asthma Approach Utilizing Evidence-Based Contemporary Guidelines

AHCCCS Pharmacy and Therapeutics Committee Meeting
May 19, 2026

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Disclosures

- Dr. Christina Kwong: I have no relevant disclosures.
- Dr. Roy Jedeikin: I have no relevant disclosures.

PCCN - At A Glance

Provider Network	Payer Partnerships	Clinical Success
1,557 *Total providers*	**+159,00** Attributed Lives	**1st** *URAC Accredited Pediatric CIN*
397 Primary Care Providers	6 Value Based Contracts	Largest Pediatric Care Management program in SW US
985 Specialist 177 Ancillary Providers	3 Commercial Value Based Agreements	Arizona's only Pediatric CIN
78 Participating TINs	3 AHCCCS / IFP Value Based Agreements	97.8% patient satisfaction for patients enrolled in care management program
195 Unique Care Locations	Direct Contracts with Whole Foods & Intel	Consistently outperforms market performance in clinical quality metrics

Phoenix Children's Care Network

PCCN 2021-2023 - Asthma Members 16,884
PCCN 4/1/25-3/31/26 - Asthma Members 7953

PCCN Asthma Pharmacy Utilization

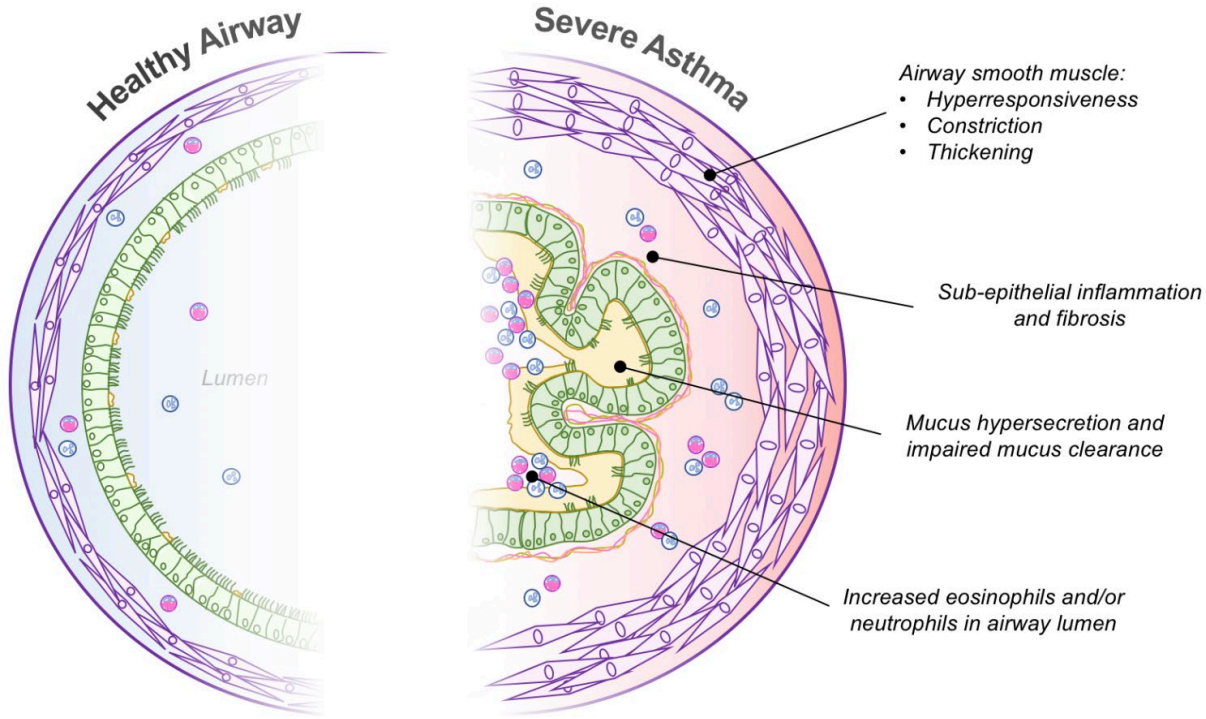
4/2024-3/2026

Category	Percent 2024	Percent 2025	Percent 2026	Overall
Other Controller	47.4%	45.3%	42.0%	45.6%
Reliever	43.0%	41.1%	42.1%	41.9%
SMART	9.6%	13.7%	16.0%	12.5%

Category	Brand	NCQA Group / Generic	Percent 2024	Percent 2025	Percent 2026	Overall
Other Controller	Flovent / Arnuity / Armonair	FLUTICASONE	21.4%	19.4%	18.1%	20.1%
Other Controller	Singulair	MONTELUKAST	11.8%	11.1%	9.5%	11.2%
Other Controller	Other Bronchodilator	BRONCHODILATOR	6.9%	6.4%	6.9%	6.6%
Other Controller	Dupixent	DUPILUMAB	3.0%	3.5%	2.8%	3.2%
Other Controller	Qvar	BECLOMETHASONE	1.9%	2.4%	2.4%	2.2%
Other Controller	Xolair	OMALIZUMAB	1.1%	1.0%	0.8%	1.0%
Other Controller	Asmanex	MOMETASONE	0.6%	0.9%	1.2%	0.8%
Other Controller	Pulmicort	BUDESONIDE	0.9%	0.5%	0.1%	0.6%
Other Controller	Alvesco	CICLESONIDE	0.1%	0.1%	0.0%	0.1%
Other Controller	Nucala	MEPOLIZUMAB	0.1%	0.1%		0.1%
Other Controller	Fasenra	BENRALIZUMAB	0.0%	0.0%	0.0%	0.0%
Other Controller	Accolate	ZAFIRLUKAST	0.0%			0.0%
Other Controller	Tezspire	TEZSPIRE			0.0%	0.0%
Reliever	Proair / Proventil / Ventolin	ALBUTEROL	42.2%	40.4%	41.5%	41.2%
Reliever	Xopenex	LEVALBUTEROL	0.6%	0.5%	0.6%	0.6%
Reliever	Airsupra	ALBUTEROL BUDESONIDE	0.0%	0.0%	0.0%	0.0%
SMART	Symbicort	SYMBICORT	7.8%	8.5%	0.3%	7.5%
SMART	Symbicort	BUDESONIDE FORMOTEROL	0.3%	3.4%	13.2%	3.1%
SMART	Breyna	BREYNA	0.8%	1.1%	1.7%	1.1%
SMART	Dulera	DULERA	0.5%	0.5%	0.7%	0.5%

Overview: What is Asthma?

- Heterogeneous disease
- Airway inflammation, bronchial hyperresponsiveness, and variable expiratory airflow limitation
- Symptoms such as cough, wheeze, chest tightness and dyspnea



Severe Asthma Toolkit. *Airway pathology in severe asthma* [figure]. severeasthma.org.au. Accessed 2025.

Asthma Burden

- 1 in 12 school-aged children have asthma in the U.S.
- 8.7% of children in Arizona have asthma
- 13.8 million missed school days per year due to asthma in the U.S.
- Over 700,000 pediatric ED visits per year in the U.S.
- The total annual cost of asthma in the United States, including medical care, absenteeism, and mortality, was $81.9 billion

Allergy & Asthma Network. Asthma Statistics Infographic. 2026.
Gogolewski G, et al. *J Clin Med.* 2025;14(22):8187.
LeCroy & Milligan Associates, Inc. ADHS Asthma Burden Report. Arizona Department of Health Services; 2025.
Nurmagambetov T, Kuwahara R, Garbe P. *Ann Am Thorac Soc.* 2018;15(3):348–356.
Pate CA, Zahran HS. The Status of Asthma in the United States. Prev Chronic Dis 2024;21:240005.

What is SMART?

- Recommended by both GINA since 2019 and NAEPP 2020
- **S**ingle **M**aintenance **A**nd **R**eliever Therapy
- **A**nti-**I**nflammatory **R**eliever (AIR) if for rescue only
- Combination ICS and formoterol – the only LABA with fast enough onset for reliever use
- Recommended for all asthma severities per GINA (2025)
- When used correctly, eliminates the need for a separate SABA inhaler

Global Initiative for Asthma. *GINA Report.* 2019. ginasthma.org Global Initiative for Asthma. *GINA Report.* 2025. ginasthma.org
NAEPP. *2020 Focused Updates to the Asthma Management Guidelines.* NHLBI; 2020.

Evidence for AIR-only with ICS-formoterol (≥12 years)

- ~10,000 patients with mild asthma
- Compared with SABA alone
  - Severe exacerbations reduced by 65%
  - ED visits/hospitalisations reduced by 65%
  - Small improvements in FEV_1, symptom control, QoL
- Compared with daily ICS + as-needed SABA
  - Similar or lower risk of severe exacerbations
  - Risk of ED visits/hospitalisations reduced by 37%
  - No clinically important differences in symptoms, lung function, quality of life
  - Very low ICS dose
  - No need for daily treatment
  - Preferred by most patients (qualitative research)
- Not just an anti-inflammatory effect
  - Benefits patients with T2-low or T2-high biomarkers
- Approved by regulators in ~50 countries

Evidence for MART with ICS-formoterol (≥12 years)

- ~30,000 patients with moderate-severe asthma
- Compared with regimens with a SABA reliever, MART reduces risk of severe exacerbations…
  - By 32% compared with same dose ICS-LABA
  - By 23% compared with higher dose ICS-LABA
  - By 17% compared with conventional best practice (in patients not required to have exacerbation history)
- Similar or better symptom control
- Lower maintenance ICS dose
- Not just an anti-inflammatory effect
  - Formoterol reduces exacerbations vs SABA, but greatest benefit is with ICS-formoterol reliever
  - Benefits patients with low or high blood eosinophils
- Approved by regulators in ~120 countries

For references, see GINA 2025 report

AIR: anti-inflammatory reliever; ED: emergency department; ICS: inhaled corticosteroid; LABA: long-acting $beta_2$-agonist; MART: maintenance-and-reliever therapy with ICS-formoterol; SABA: short-acting $beta_2$-agonist

SMART Reduces Exacerbation Risk in Pediatric Patients

- 12 years and older: SMART reduces severe exacerbations by 23–32% vs. ICS-LABA + SABA, and by 65% vs. SABA alone
- Younger children: two randomized controlled trials, reduced exacerbations by 45–75%
- Both GINA 2025 and NAEPP 2020 endorse ICS-formoterol for children as young as 4 years

Bisgaard H, et al. J Allergy Clin Immunol. 2006;118(2):411–418.
GINA. Global Strategy for Asthma Management and Prevention. 2025. ginasthma.org
Hatter L, et al. Lancet. 2025;406(10511):1473–1483.
NAEPP. *2020 Focused Updates to the Asthma Management Guidelines.* NHLBI; 2020.

Symptoms (suggestions)	Treatment Step	Children 6-11 years *MART: Budesonide-formoterol 80/4.5: MAX 8 inh per day	Adolescents 12 and up *AIR/MART: Budesonide-formoterol 160/4.5 MAX 12 inh per day
Infrequent (1-2 days per week or less)	Step 1	PRN ICS and SABA	AIR 1 inhalation as needed
6-11 years: 2-5 days per week **≥12 years**: <3-5 days per week, normal or mildly reduced lung function	Step 2	Daily ICS, PRN SABA	AIR 1 inhalation as needed
Asthma symptoms most days, waking up at night once a week or more **≥12 years only**: or low lung function	Step 3	• Low dose daily ICS + PRN SABA • Med dose daily ICS + PRN SABA • Very low dose: 1 inhalation once daily **MART** + 1 as needed	**MART** Very Low or Low dose: 1 inhalation 1-2 times a day + 1 as needed
Daily asthma symptoms, waking up at night once a week or more, with low lung function	Step 4	• Medium dose daily ICS-LABA + PRN SABA • Low dose **MART** 1 inhalation twice daily + 1 as needed	**MART** Medium dose: 2 inhalation twice daily + 1 as needed
	Step 5	Refer for phenotypic assessment +/- higher dose	**MART** Medium/high dose: 2 inhalations twice daily + 1 as needed

GINA. Global Strategy for Asthma Management and Prevention. 2025. ginasthma.org

SABA Overuse: A Common and Dangerous Pattern

- SABA-only use is not recommended per GINA – does not treat underlying inflammation and is associated with worse lung function
- ≥3 canisters/year → increased risk of severe exacerbations (HR 1.26)
  - MO HealthNet: at least 40.5% of participants received 3 or more canisters in 2021
- ≥11 canisters/year → 2.35x higher mortality risk vs. appropriate SABA use
  - MO HealthNet: 6.4% of participants met this threshold in 2021

Bloom CI, et al. *Eur Respir J.* 2020;55(4):1901872.
GINA. Global Strategy for Asthma Management and Prevention. 2025. ginasthma.org
Moore J. *Advancing Appropriate Medication Therapy by Practice and Policy.* MO HealthNet; 2022.
Morgan A, et al. *ERJ Open Res.* 2023;9:00571-2022.

OCS Harms: Single-Course Effects

- When airway inflammation, mucus hypersecretion, and bronchoconstriction are severe:
  - Inhaled corticosteroids cannot reliably penetrate the obstructed airway lumen.
  - Oral corticosteroids (OCS) are needed to reach airway tissue via systemic circulation — but this comes at the cost of exposure to the adrenal glands, bone, brain, gut, and immune system.
- **Even a single OCS burst is associated with a 1.4- to 2.2-fold increased risk of GI bleeding, sepsis, and pneumonia** — risk is highest in the first 30 days
  - From a nationwide study of 4.5 million Taiwanese children; 1 million+ received OCS, most commonly for respiratory infections and allergic diseases
- Common symptoms: irritability, mood swings, sleep disturbance, hyperactivity, increased appetite, GI upset

Derendorf H, et al. *Eur Respir J.* 2006;28(5):1042–1050.
Warrington TP, Bostwick JM. *Mayo Clin Proc.* 2006;81(10):1361–1367.
Yao TC, et al. *JAMA Pediatr.* 2021;175(7):723–729.

OCS Harms: Long-Term Effects

- Adults:
  - ≥4 courses/year → dose-dependent increased risk of osteoporosis, HTN, DM, GI ulcers/bleeds, fractures, heart failure, and cataracts
- Children:
  - In 65,000+ children with persistent asthma, ≥4 OCS courses/year was associated with 2.9x higher odds of complications, **6.9x more asthma hospitalizations, and 5.0x more ED visits** compared to no OCS exposure
  - ≥2 courses/year → measurable growth suppression in longitudinal studies
  - ≥4 courses/year → dose-dependent fracture risk; adrenal suppression
  - Repeated cycles associated with cognitive effects, mood disturbance, and risk of psychotic symptoms

Dolan LM, et al. *J Allergy Clin Immunol.* 1987;80(4):488–496.
GINA. Global Strategy for Asthma Management and Prevention. 2025. ginasthma.org
Ji H, et al. *Pediatr Allergy Immunol.* 2025;36(7):e70143.
Mrakotsky C, et al. *J Int Neuropsychol Soc.* 2013;19(1):96–109.
Stuart FA, et al. *Arch Dis Child.* 2005;90(5):500–506.
Sullivan PW, et al. *J Allergy Clin Immunol Pract.* 2021;9(4):1541–1551.
Zeiger R, et al. *J Allergy Clin Immunol Pract.* 2020;8(10):3455–3465.

How can we make SMART happen?

- **Coverage of two ICS-formoterol inhalers per month, without prior authorization or step therapy requirements**
- Guideline awareness and implementation education for providers, patients, and families

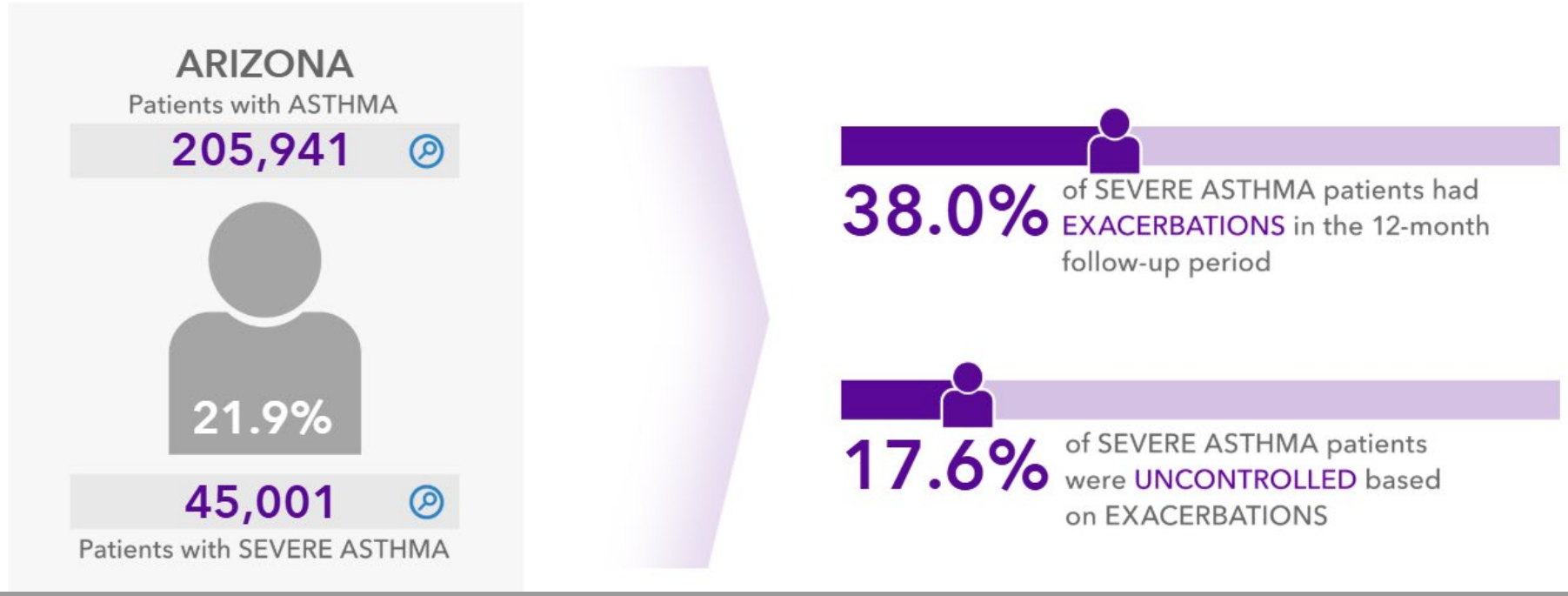
Arizona Data for Patients with Severe Asthma

MEDICATION USE

Additional asthma medication use among patients with SEVERE ASTHMA

	ARIZONA	Male	Female	Age 12-17	18-64	65+	White	Black	Hispanic	Other*
Biologics	6.9%	5.7%	7.5%	11.7%	6.6%	5.8%	6.2%	13.3%	7.2%	6.9%
Systemic corticosteroids	63.6%	54.1%	68.5%	56.9%	64.1%	64.0%	60.3%	65.0%	70.4%	64.4%

EpiCentral. *Asthma Heatmap Tool.* us.epicentralmed.com. Accessed 2026.



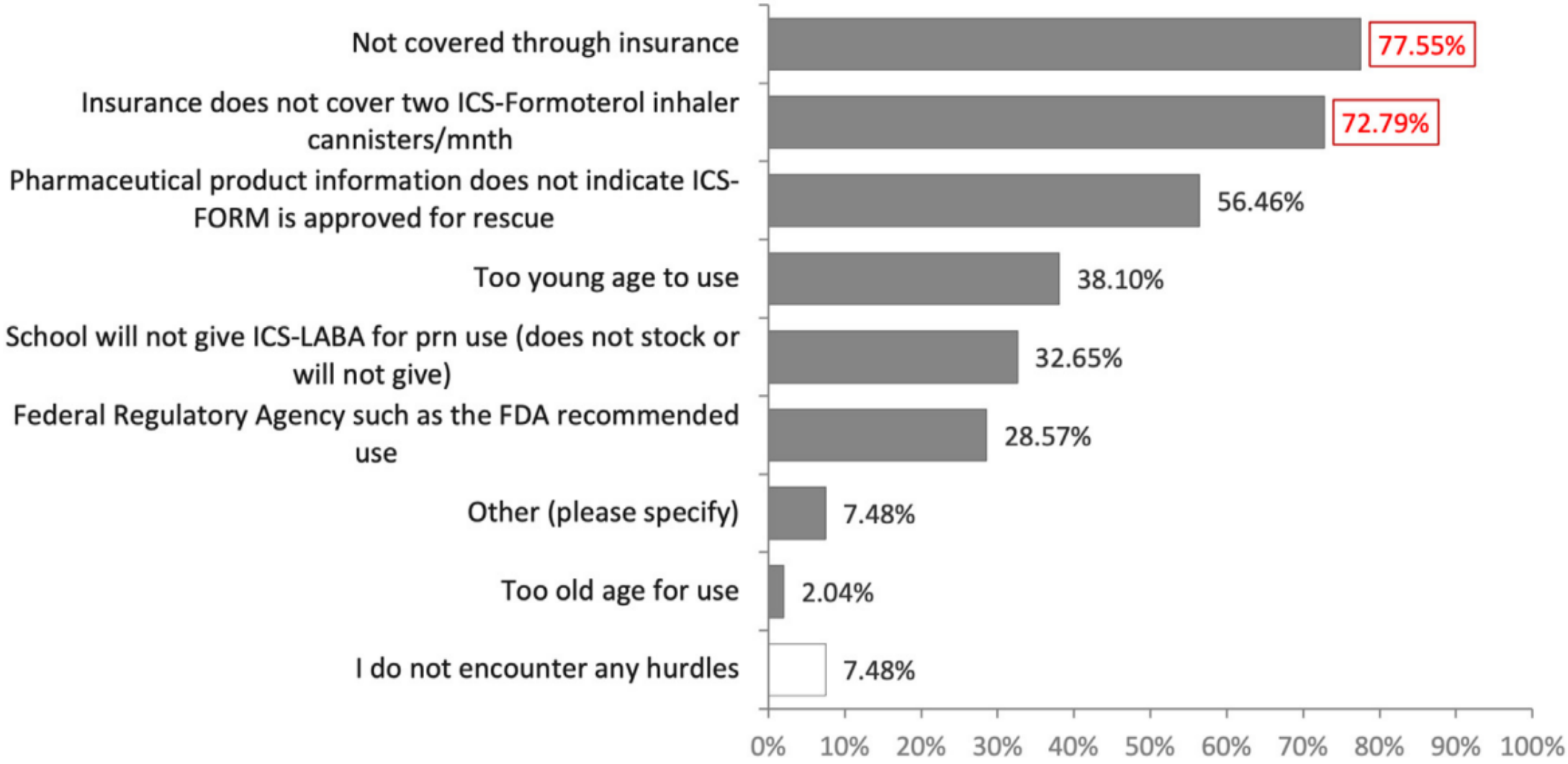
INPATIENT CARE

Proportion of patients with EXACERBATIONS who required HOSPITALIZATIONS or ER VISITS

ARIZONA	Male	Female	Age 12-17	18-64	65+	White	Black	Hispanic	Other*
14.6%	14.8%	14.4%	20.0%	15.8%	10.4%	10.6%	NA	17.8%	15.8%

EpiCentral. *Asthma Heatmap Tool.* us.epicentralmed.com. Accessed 2026.

Hurdles for prescribing one's preferred ICS-formoterol use



Bacharier LB. *Presidential Plenary: Trending Topics in Allergy and Immunology.* ACAAI Annual Meeting; 2023.

PCCN Survey: SMART/AIR Medication Barriers

Top barrier: Insurance Coverage (37 out of 41)

Second highest: Medication Cost (28 out of 41)

Third highest: Education on Latest Guidelines (15 out of 41)

A Call for the United States to Accelerate the Implementation of Reliever Combination Inhaled Corticosteroid–Formoterol Inhalers in Asthma

Krings JG et al. A Call for the United States to Accelerate the Implementation of Reliever Combination Inhaled Corticosteroid-Formoterol Inhalers in Asthma. Am J Respir Crit Care Med. 2023 Feb 15;207(4):390-405

- Every study of SMART has used **ICS–formoterol**, which also has a dose–response relationship that **safely** allows for repeated inhalations if necessary
- A reliever-only budesonide–formoterol treatment approach was more **beneficial** than traditional maintenance ICS plus reliever SABA at preventing severe asthma exacerbations
- In **mild asthma, a reliever-only ICS–formoterol** approach leads to **lower cumulative inhaled corticosteroid exposure** than traditional **maintenance ICS plus reliever SABA therapy**
- SMART with ultra-low–dose budesonide–formoterol (80/4.5 μg one puff daily and for symptoms) was investigated **in children (age 4–11 yr)** and **significantly reduced the rate of exacerbations in this population**
- Both GINA [Global Initiative for Asthma]) and NAEPP [National Asthma Education and Prevention Program]) have clearly advocated for SMART
- Pharmaceutical formulary practices are a particular obstacle for SMART therapy
- **Barrier:** if a patient uses two puffs twice daily of budesonide–formoterol and the same inhaler on a reliever basis, they could run out of their 120-actuation inhaler before the end of the month when they are eligible for a refill
- **Conclusion: “Nonetheless, we currently have an opportunity to radically change how we treat asthma and reduce some of the preventable burdens our patients face”**

Thank you!

We welcome any questions or comments.

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Welcome and Introductions

- Suzi Berman, RPh, Pharmacy Director, AHCCCS
  - Minutes Review and Vote - P&T January 13, 2026
  - Review
  - Vote

Prime Therapeutics Class Reviews

Classes for Review: Supplemental Rebate Classes

- Antibiotics, Inhaled
- Antimigraine Agents, Other
- Antipsychotics, Atypical Injectable
- Antipsychotics, Oral Atypical (2nd Gen Only)
- Colony Stimulating Factors
- COPD Agents
- Cytokine and CAM Antagonists
- GI Motility, Chronic
- Glucagon Agents
- Growth Hormone
- Hepatitis C Agents
- Hypoglycemics, Incretin Mimetics/Enhancers
- Immunologics (Immunomodulators, Atopic Dermatitis and Immunomodulators, Asthma)
- Movement Disorders
- Multiple Sclerosis Agents
- Opioid Dependence Treatments
- Pancreatic Enzymes
- Uterine Disorder Treatments

Prime Therapeutics Drug Class Reviews

Hind Douiki, PharmD

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Antibiotics, Inhaled

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Antibiotics, Inhaled

Class Overview: Products

- Arikayce (amikacin liposome)
- Bethkis (tobramycin)
- Cayston (aztreonam)
- Kitabis Pak (tobramycin)
- Tobi (tobramycin)
- Tobi Podhaler (tobramycin)
- tobramycin pak (tobramycin)
- tobramycin solution (tobramycin)

Antibiotics, Inhaled

- Inhaled antibiotics are used in the treatment of Cystic Fibrosis
- CF is an autosomal recessive disorder caused by mutations of the cystic fibrosis transmembrane conductance regulator (CFTR) gene located on chromosome number 7
- CF affects close to 40,000 individuals in the U.S.
- It involves progressive obstructive lung disease associated with impaired mucous clearance, difficulty clearing pathogens, and risk of chronic pulmonary infection and inflammation
- As pulmonary infection is the main source of morbidity and mortality, antibiotics play an important role to control the progression of the disease

Antibiotics, Inhaled

- The 2014 Cystic Fibrosis Foundation (CFF) guidelines recommend inhaled antibiotic therapy for the treatment of P. aeruginosa, with preference for tobramycin
- Inhaled tobramycin and inhaled aztreonam are recommended in the 2013 CF Pulmonary guidelines to reduce exacerbation for patients who are ≥ 6 years of age with persistent P. aeruginosa cultures in the airways
- In patients with pulmonary exacerbations marked by chronic infection of P. aeruginosa, treatment with the combination of aminoglycoside and beta-lactam antibiotic is recommended

Antibiotics, Inhaled

- Alternate-month administration of both tobramycin and aztreonam is recommended in patients persistently infected with P. aeruginosa
- In 2016, a clinical guideline for CF in preschool-aged children was developed by the CFF
- CFF recommends oral, inhaled, and/or IV antibiotics for treatment of pulmonary exacerbations and every other month inhaled antibiotics in patients with persistent P. aeruginosa infection
- In 2020, the CFF released recommendation statements regarding the treatment of advanced cystic fibrosis lung disease
- This includes a trial of alternating inhaled antibiotics in a continuous manner as dictated by the bacterial isolates found in respiratory culture

Antibiotics, Inhaled

- *Mycobacterium avium* complex (MAC) is the most common nontuberculous mycobacterial (NTM) lung infection
- In 2020 the American Thoracic Society (ATS), European Respiratory Society (ERS), European Society of Clinical Microbiology and Infectious Diseases (ESCMID), and Infectious Diseases Society of America (IDSA) published a clinical practice guideline on the treatment of NTM pulmonary disease
- They recommend Arikayce in adults with limited or no alternative treatment options for MAC lung disease as part of a combination antibacterial drug regimen
- An IV aminoglycoside should only be included in the initial treatment regimen for select patients
- If patients with MAC pulmonary disease have failed ≥ 6 months of therapy, the addition of amikacin liposome inhalation suspension (ALIS) to the current regimen is recommended over a standard oral regimen only

Antimigraine Agents, Other

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Antimigraine Agents, Other

Drug	Manufacturer	Other Indications
Calcitonin gene-related peptide (CGRP) antagonists		
atogepant (Qulipta)	Abbvie	Preventive treatment of migraine in adults
eptinezumab-jjmr (Vyepti)	Lundbeck Seattle	Preventive treatment of migraine in adults
erenumab-aooe (Aimovig)	Amgen	Preventive treatment of migraine in adults
fremanezumab-vfrm (Ajovy)	Teva	Preventive treatment of migraine in adults Preventive treatment of episodic migraine in pediatric patients who are 6 to 17 years of age and who weigh 45 kg or more
galcanezumab-gnlm (Emgality)	Eli Lilly	Preventive treatment of migraine in adults Treatment of episodic cluster headache in adults
rimegepant (Nurtec® ODT)	Biohaven/Pfizer	Acute treatment of migraine with or without aura in adults Preventive treatment of episodic migraine in adults
ubrogepant (Ubrelvy)	Allergan	Acute treatment of migraine with or without aura in adults
zavegepant (Zavzpret)	Pfizer	Acute treatment of migraine with or without aura in adults
Serotonin (5-HT) 1F receptor agonist		
lasmiditan (Reyvow)	Eli Lilly	Acute treatment of migraine with or without aura in adults

Antimigraine Agents, Other

- Migraines account for 10% to 20% of all headaches in adults and affect over 37 million individuals in the U.S.
- Prevalence of migraine may exceed 20% in adolescents
- Non-opioid analgesia with a nonsteroidal anti-inflammatory drug (NSAID), or combinations such as aspirin or acetaminophen plus caffeine, are recommended as first-line therapy for patients with mild to moderate migraine pain
- If these therapies fail, or if the patient experiences moderate-to-severe attacks, AHS recommends triptans, dihydroergotamine (DHE), calcitonin gene-related peptides (CGRPs), or selective serotonin (5-HT1F) receptor agonist
- Nurtec ODT, Ubrelvy, Zavzpret, and Reyvow are approved for the acute treatment of migraine with or without aura in adults

Antimigraine Agents, Other

- Evidence suggests that 40% of people who experience migraines are candidates for preventative therapy
- Cluster headache (CH) is a severe, primary headache disorder characterized by extreme pain on one side of the head and autonomic symptoms
- CH periods can persist for weeks to months with daily or more frequent attacks of 15 to 180 minutes in duration
- CH can be either episodic or chronic in nature with episodic CH being the predominant form
- Patients with episodic CH experience periods of attack followed by periods of remission
- Patients with chronic CH have minimal to no periods of remission between headache attacks

Antimigraine Agents, Other

- Per the 2024 AHS, the following are recommended as first-line treatment options for prevention of episodic and chronic migraines:
  - CGRP antagonists
  - Some antiepileptics (topiramate, divalproex sodium, sodium valproate)
  - Various beta blockers (metoprolol, propranolol, timolol, atenolol, nadolol)
  - Candesartan
  - Certain antidepressants (amitriptyline, nortriptyline, venlafaxine, duloxetine)
- OnabotulinumtoxinA (Botox) is listed as a first-line option for the prevention of chronic migraine only
- There are limited head-to-head trials of CGRP antagonists in migraine prevention therapies

Antimigraine Agents, Other

- AHS states that treatment for acute attaches and for migraine prevention should be individualized to the patient
- The 2016 AHS guidelines recommended the following for the treatment of CH:
  - Sumatriptan SC, zolmitriptan nasal spray, and 100% oxygen for the acute treatment of episodic or chronic CH
  - Therapies considered probably effective for episodic and chronic CH include sumatriptan nasal spray and oral zolmitriptan
  - Galcanezumab-gnlm (Emgality) is FDA-approved for episodic CH that decreases the frequency of acute attacks and was not available at the time of this guideline development

Antimigraine Agents, Other

Product/Guideline Update

- Reyvow has been discontinued in 2025
- Medication is expected to be available until June 2026
- There are no available generics

Antipsychotics

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Antipsychotics

Class Overview - Product indications include, but are not limited to:

- Schizophrenia, bipolar disorder, major depressive order, schizoaffective disorder, irritability associated with autism, Tourette’s disorder, agitation associated with Alzheimer’s Disease, Parkinson's disease psychosis

Antipsychotics

- Schizophrenia affects ~1.2% to 1.8% of adults in the U.S.
- Inconclusive evidence remains regarding the overall effectiveness of second generation antipsychotics compared to first generation agents
- Second generation antipsychotics are associated with less extrapyramidal symptoms (EPS) than first generation agents
- The question of long-term adverse events with second generation antipsychotic use remains unresolved
- Second generation antipsychotics have largely replaced first generation antipsychotics in the treatment of psychotic disorders
- However, the long-term effectiveness and adverse event profiles of these products have not been shown to be definitively superior

Antipsychotics

- Inconclusive data exists to indicate which second generation antipsychotic agent to use first
- Clozapine is used for patients with treatment-resistant schizophrenia and in patients with recurrent suicidal behavior at high risk of suicide
- Clozapine is reserved for refractory patients due to rare reports of severe neutropenia and seizures
- Various guidelines exist to help in choosing the best individualized treatment for schizophrenia, bipolar disorder, or major depressive disorder
- Relative occurrences of adverse events may also be considered in product selection

Antipsychotics Atypical Injectable

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Antipsychotics, Atypical Injectable

Drug	Manufacturer	Other Indications	Schizophrenia	Bipolar Disorder
Second Generation Antipsychotics – Long Acting Injectable				
aripiprazole ER (Abilify Asimtufii®)	Otsuka		X	X (maintenance treatment as monotherapy)
aripiprazole ER (Abilify Maintena®)	Otsuka	--	X	X (maintenance treatment as monotherapy)
aripiprazole lauroxil ER (Aristada™)	Alkermes	--	X	--
aripiprazole lauroxil ER (Aristada Initio™)	Alkermes	--	X (for initial dose or select missed doses only)	--
olanzapine (Zyprexa® Relprevv)	Eli Lilly	--	X	--
paliperidone palmitate (Invega Sustenna®) (Erzofri®)	Janssen Shandong Luye	Schizoaffective disorder (monotherapy and as an adjunct to mood stabilizers or antidepressants)	X	--

Antipsychotics, Atypical Injectable

Drug	Manufacturer	Other Indications	Schizophrenia	Bipolar Disorder
Second Generation Antipsychotics – Long Acting Injectable				
paliperidone palmitate (Invega Trinza®)	Janssen	--	X (treatment in patients after they have been adequately treated with Invega Sustenna for ≥ 4 months)	--
paliperidone palmitate (Invega Hafyera™)	Janssen		X (treatment in patients after they have been adequately treated with Invega Sustenna for ≥ 4 months or Invega Trinza for ≥ one 3-month cycle)	
risperidone microspheres (Risperdal Consta®) (Rykindo®)	generic, Janssen Shandong Luye	--	X	X (maintenance treatment as monotherapy or in combination with lithium or valproate)
risperidone ER suspension (Perseris™)	Indivior	--	X	--
risperidone ER suspension (Uzedy™)	Teva Neuroscience	--	X	X (monotherapy or as adjunctive therapy to lithium or valproate for maintenance treatment of bipolar I disorder)

Antipsychotics, Atypical Injectable

Drug	Manufacturer	Other Indications	Schizophrenia	Bipolar Disorder
Second Generation Antipsychotics – Short Acting Injectable				
olanzapine	generic	Acute agitation associated with schizophrenia or bipolar mania	--	--
ziprasidone (Geodon®)	generic, Pfizer/Viatris	—	X (acute agitation)	—

Antipsychotics, Atypical Long-Acting Injectable

- There are not enough comparative data to support distinctions among the injectable second generation antipsychotics
- A meta-analysis evaluated the impact of long-acting injectable antipsychotic frequency on efficacy and other outcomes
- No differences were found in psychotic symptoms or quality of life between injectables dosed every 2 or 4 weeks
- Safety analyses were also very similar, except for injection-site pain, which was lower with every 2-week formulations compared to every 4-week formulations
- Overall, data is very limited

Antipsychotics Second Generation Oral

ARIZONA HEALTH CARE COST CONTAINMENT SYSTEM

Antipsychotics, Second Generation Oral

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

Antipsychotics, Second Generation Oral

Drug	Manufacturer	Other Indications	Schizophrenia	Bipolar Disorder			
				Acute Manic Episodes	Depressive Episodes	Acute Mixed Episodes	Maintenance
Second Generation Antipsychotics – Oral							
asenapine (Saphris®)	generic, Forest/ Allergan	--	X	X (ages ≥ 10 years for acute treatment as monotherapy; adults in combination with lithium or valproate)	--	X (ages ≥ 10 years for acute treatment as monotherapy; adults in combination with lithium or valproate)	X (monotherapy; adults only)
brexpiprazole (Rexulti®)	Otsuka	Major depressive disorder (adjunct); agitation associated with Alzheimer's dementia‡	X	--	--	--	--
cariprazine (Vraylar™)	Allergan	Major depressive disorder (adjunct)	X	X (acute treatment)	X	X (acute treatment)	--

Antipsychotics, Second Generation Oral

Drug	Manufacturer	Other Indications	Schizophrenia	Bipolar Disorder			
				Acute Manic Episodes	Depressive Episodes	Acute Mixed Episodes	Maintenance
Second Generation Antipsychotics – Oral							
clozapine (Clozaril®)	Generic Novartis/HLS	--	X (treatment-resistant schizophrenia; reducing suicidal behavior in schizophrenia or schizoaffective disorder	--	--	--	--
clozapine orally disintegrating tablets (ODT)	Generic						
clozapine (Versacloz®)	Trupharma						

Antipsychotics, Second Generation Oral

Drug	Manufacturer	Other Indications	Schizophrenia	Bipolar Disorder			
				Acute Manic Episodes	Depressive Episodes	Acute Mixed Episodes	Maintenance
Second Generation Antipsychotics – Oral							
iloperidone (Fanapt®)	Vanda	--	X	X	--	--	--
lumateperone (Caplyta®)	Intra-Cellular Therapies	X adjunctive treatment with antidepressants for MDD	X	--	--	--	--
lurasidone (Latuda®)	generic, Sunovion	--	X (ages ≥ 13 years)	--	X (ages ≥10 years as monotherapy and in combination with lithium or valproate)	--	--
olanzapine (Zyprexa®)	Generic, H2 Pharma	X Treatment-resistant depression (in combination with fluoxetine)	X (ages ≥ 13 years; second-line in adolescents due to metabolic effects)	X (ages ≥ 13 years as monotherapy and in combination with lithium or valproate; second-line in adolescents due to metabolic effects)	X (ages ≥ 10 years; in combination with fluoxetine)	X (ages ≥ 13 years as monotherapy and in combination with lithium or valproate; second-line in adolescents due to metabolic effects)	X (ages ≥ 13 years)

Antipsychotics, Second Generation Oral

Drug	Manufacturer	Other Indications	Schizophrenia	Bipolar Disorder			
				Acute Manic Episodes	Depressive Episodes	Acute Mixed Episodes	Maintenance
Second Generation Antipsychotics – Oral							
olanzapine/ fluoxetine	Generic, Eli Lilly	Treatment-resistant depression	--	--	X (ages ≥ 10 years for acute episodes)	--	--
olanzapine/ samidorphan (Lybalvi™)	Alkermes		X	X (monotherapy and in combination with lithium or valproate)		X (monotherapy and in combination with lithium or valproate)	X (monotherapy)
paliperidone ER (Invega®)	Generic, Janssen	Schizoaffective disorder (monotherapy or adjunct with mood stabilizers and/or antidepressants)	X (ages ≥ 12 years)	--	--	--	--
pimavanserin (Nuplazid™)	Acadia	Hallucinations and delusions associated with Parkinson's disease (PD) psychosis	--	--	--	--	--

Antipsychotics, Second Generation Oral

Drug	Manufacturer	Other Indications	Schizophrenia	Bipolar Disorder			
				Acute Manic Episodes	Depressive Episodes	Acute Mixed Episodes	Maintenance
Second Generation Antipsychotics – Oral							
quetiapine (Seroquel®)	generic, AstraZeneca	--	X (ages ≥ 13 years)	X (ages ≥ 10 years as monotherapy; adults in combination with lithium or valproate)	X	--	X (in combination with lithium or divalproex)
quetiapine ER (Seroquel XR®)	generic., AstraZeneca	Major depressive disorder (adjunct)	X (ages ≥ 13 years)	X (ages ≥ 10 years as monotherapy; adults in combination with lithium or valproate)	X	X (ages ≥ 10 years as monotherapy; adults in combination with lithium or valproate)	X (in combination with lithium or divalproex)

Antipsychotics, Second Generation Oral

Drug	Manufacturer	Other Indications	Schizophrenia	Bipolar Disorder			
				Acute Manic Episodes	Depressive Episodes	Acute Mixed Episodes	Maintenance
Second Generation Antipsychotics – Oral							
risperidone (Risperdal®)	generic, Janssen	Irritability associated with autistic disorder (ages 5-17 years)	X (ages ≥ 13 years)	X (ages ≥ 10 years as monotherapy; adults in combination with lithium or valproate)	--	X (ages ≥ 10 years as monotherapy; adults in combination with lithium or valproate)	--
xanomeline/ trospium (Cobenfy®	BMS		X				X
ziprasidone (Geodon®)	generic., Pfizer/Viatris	--	X	X (acute episodes)	--	X (acute episodes)	X (in combination with lithium or divalproex)

Antipsychotics, Second Generation Oral

Product/Guideline Updates:

- The FDA approved a new oral film formulation of aripiprazole, Mezofy
- It is indicated for the treatment of schizophrenia in patients ≥ 13 years of age
- FDA has approved Bysanti for treatment of schizophrenia in adults and for acute treatment of manic or mixed episodes associated with bipolar I disorder in adults

Colony Stimulating Factors

ARIZONA
HEALTH CARE COST
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Colony Stimulating Factors

Drug	Manufacturer	Cancer patients receiving myelosuppressive chemotherapy *(To reduce incidence of infection [febrile neutropenia])*	Acute Myeloid Leukemia (AML) patients receiving chemotherapy *(Following induction or consolidation chemotherapy to reduce time to neutrophil recovery and the duration of fever in adults)*	Bone Marrow Transplant (BMT)	Peripheral Blood Progenitor Cell (PBPC) Collection and Therapy	Severe Chronic Neutropenia *(To reduce the incidence and duration of neutropenia in symptomatic patients with congenital neutropenia, cyclic neutropenia, or idiopathic neutropenia)*	Hematopoietic Syndrome of Acute Radiation Syndrome *(To increase survival in patients acutely exposed to myelosuppressive doses of radiation)*
efbemalenograstim alfa-vuxw (Ryzneuta®)[1]	Acrotech	X	--	--	--	--	--
eflapegrastim-xnst (Rolvedon®)[2]	Spectrum	X	--	--	--	--	--
filgrastim (Neupogen®)[3]	Amgen	X	X	X[a]	X	X	X
filgrastim-aafi (Nivestym®)*[4]	Pfizer	X	X	X[a]	X	X	--
filgrastim-ayow (Releuko®)*[5]	Amneal	X	X	X[a]	X	X	X
filgrastim-sndz (Zarxio®)*[6]	Sandoz	X	X	X[a]	X	X	X
filgrastim-txid (Nypozi®)*[7]	Tanvex	X	X	X[a]	X	X	X
pegfilgrastim (Neulasta®)[8]	Amgen	X	--	--	--	--	X
pegfilgrastim-apgf (Nyvepria®)†[9]	Pfizer	X	--	--	--	--	--

Colony Stimulating Factors

Drug	Manufacturer	**Cancer patients receiving myelosuppressive chemotherapy** *(To reduce incidence of infection [febrile neutropenia])*	**Acute Myeloid Leukemia (AML) patients receiving chemotherapy** *(Following induction or consolidation chemotherapy to reduce time to neutrophil recovery and the duration of fever in adults)*	**Bone Marrow Transplant (BMT)**	**Peripheral Blood Progenitor Cell (PBPC) Collection and Therapy**	**Severe Chronic Neutropenia** *(To reduce the incidence and duration of neutropenia in symptomatic patients with congenital neutropenia, cyclic neutropenia, or idiopathic neutropenia)*	**Hematopoietic Syndrome of Acute Radiation Syndrome** *(To increase survival in patients acutely exposed to myelosuppressive doses of radiation)*
pegfilgrastim-cbqv (Udenyca®)†[10]	Coherus	X	--	--	--	--	X
pegfilgrastim-jmdb (Fulphila®)†[11]	Mylan/Biocon	X	--	--	--	--	--
pegfilgrastim-bmez (Ziextenzo®)†[12]	Sandoz	X	--	--	--	--	X
pegfilgrastim-fpgk (Stimufend®)†[13]	Fresenius Kabi	X	--	--	--	--	X
pegfilgrastim-pbbk (Fylnetra®)†[14]	Amneal	X	--	--	--	--	X
sargramostim (Leukine®)[15]	Partner	--	X	X[b]	X	--	X
tbo-filgrastim (Granix®)[16]	Cephalon/Teva	X	--	--	--	--	--

Colony Stimulating Factors

- Colony stimulating factors (CSF) are hematopoietic growth factors that have been shown to decrease the likelihood of chemotherapy-induced neutropenic complications and to improve relative chemotherapy dose intensity
- Prophylactic CSF use can reduce the severity, risk, and duration of febrile neutropenia and decrease rates of infection
- Efbemalenograstim alfa-vuxw (Ryzneuta), eflapegrastim-xnst (Rolvedon), filgrastim (Neupogen), filgrastim-aafi (Nivestym), filgrastim-ayow (Releuko), filgrastim-sndz (Zarxio), filgrastim-txid (Nypozi), pegfilgrastim (Neulasta), pegfilgrastim-apgf (Nyvepria), pegfilgrastim cbqv (Udenyca), pegfilgrastim-jmdb (Fulphila), pegfilgrastim-bmez (Ziextenzo), pegfilgrastimfpgk (Stimufend), pegfilgrastim-pbbk (Fylnetra), and tbo-filgrastim (Granix) are granulocyte colony-stimulating factors (G-CSF)

Colony Stimulating Factors

- Sargramostim (Leukine) is a granulocyte-macrophage colony stimulating factor (GM-CSF)
- The administration frequency of pegfilgrastim and its biosimilars may be viewed as more favorable since these only require a single SC injection per chemotherapy cycle
- Filgrastim products and sargramostim (Leukine) administration require daily subcutaneous injection
- Several biosimilars are now available to the originator products, filgrastim and pegfilgrastim

Colony Stimulating Factors

- The NCCN v1.2026 practice guidelines for hematologic growth factors indicate subcutaneous filgrastim, tbo-filgrastim, and pegfilgrastim have a category 1 recommendation that they prophylactically reduce the risk of febrile neutropenia
- The guidelines advise caution should be used with prophylactic use of G-CSFs administered with chemotherapy and radiation concurrently
- Sargramostim is no longer recommended for prophylactic use in patients with solid tumors receiving myelosuppressive chemotherapy

Colony Stimulating Factors

- The guidelines note that a biosimilar is a biological product that is highly similar to the FDA-approved originator product with very small, clinically inactive differences but no difference in efficacy, safety, or purity
- NCCN states limited data suggest that patients can alternate between the originator product and the biosimilar without any clinically meaningful differences regarding efficacy or safety
- Eflapegrastim-xnst (Rolvedon) and efbemalenograstim alfa-vuxw (Ryzneuta) are included in the guideline as category 2A recommendations

Colony Stimulating Factors

- NCCN guidelines recommend that high-risk patients receive prophylactic CSF regardless of the treatment intent
- For intermediate-risk patients, NCCN recommends individualized consideration of CSF based on the likelihood of developing febrile neutropenia, consequences of developing febrile neutropenia, and the implications of interfering with chemotherapy treatments
- NCCN does not recommend the routine use of CSF in patients with low risk of developing febrile neutropenia
- The guidelines advise against use of G-CSFs within 14 days after receipt of chimeric antigen receptor-modified T cell (CAR-T) therapy
- Use after this time period is considered for treatment of neutropenia

Colony Stimulating Factors

- Per NCCN, there is less evidence to support the CSFs for therapeutic use for febrile neutropenia and should be considered only in select patients
- If therapeutic use is indicated, then CSF should be considered
- Filgrastim, filgrastim biosimilars, tbo-filgrastim, and sargramostim have a 2A recommendation for therapeutic use
- Pegfilgrastim, its biosimilars, eflapegrastim-xnst, and efbemalenograstim alfa-vuxw have only been studied for prophylactic use

Colony Stimulating Factors

Product/Guideline Updates:

- FDA has approved two new indications for Releuko:
  - (1) Mobilize autologous hematopoietic progenitor cells into the peripheral blood for collection by leukapheresis
  - (2) Increase survival in patients acutely exposed to myelosuppressive doses of radiation (Hematopoietic Syndrome of Acute Radiation Syndrome)
- Teva will discontinue Granix 480 mcg/1.6 mL injection

Colony Stimulating Factors

Product/Guideline Updates:

- FDA has approved pegfilgrastim-unne (Armlupeg) as a biosimilar to pegfilgrastim (Neulasta)
- Will be supplied as a 6 mg/0.6 mL injection for SC use in a single-dose prefilled syringe
- Armlupeg is indicated to:
    - (1) Decrease the incidence of infection, as manifested by febrile neutropenia, in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a clinically significant incidence of febrile neutropenia
    - (2) Increase survival in patients acutely exposed to myelosuppressive doses of radiation

Colony Stimulating Factors

Product/Guideline Updates:

- FDA has approved filgrastim-laha (Filkri) as biosimilar to filgrastim (Neupogen)
- Approved as a 300 mcg/0.5 mL injection for SC or IV use in a single-dose PFS and a 480 mg/0.8 mL injection for SC or IV use in a single-dose PFS
- Filkri is indicated for:
    - (1) Patients with cancer receiving myelosuppressive chemotherapy
    - (2) Patients with AML receiving induction or consolidation chemotherapy
    - (3) Patients with cancer undergoing bone marrow transplantation
    - (4) Patients with severe chronic neutropenia
    - (5) Patients acutely exposed to myelosuppressive doses of radiation (hematopoietic syndrome of acute radiation syndrome)

COPD Agents

ARIZONA
HEALTH CARE COST
CONTAINMENT SYSTEM

COPD Agents

Class Overview: Antimuscarinics – Short-Acting

- ipratropium inhalation aerosol - (Atrovent HFA)
- ipratropium inhalation solution - (ipratropium inhalation solution)

Class Overview: Antimuscarinics – Long-Acting

- aclidinium bromide - (Tudorza Pressair)
- glycopyrrolate - (Lonhala Magnair)
- tiotropium bromide inhalation spray - (Spiriva Respimat)
- tiotropium inhalation powder - (Spiriva HandiHaler)
- umeclidinium - (Incruse Ellipta)
- revefenacin - (Yupelri)

COPD Agents

Class Overview: Beta Agonist/Antimuscarinic Combination – Short-Acting

- albuterol/ipratropium MDI CFC-Free - (Combivent Respimat)
- albuterol/ipratropium inhalation solution - (albuterol/ipratropium inhalation solution)

Class Overview: Beta Agonist/Antimuscarinic Combination – Long-Acting

- aclinidium bromide/formoterol - (Duaklir Pressair)
- formoterol/glycopyrrolate - (Bevespi Aerosphere)
- tiotropium/olodaterol - (Stiolto Respimat)
- umeclidinium/vilanterol - (Anoro Ellipta)

COPD Agents

Class Overview: Phosphodiesterate 4 (PDE-4) Inhibitor

- roflumilast - (Daliresp)

Class Overview: **Phosphodiesterase 3,4 (PDE3 and PDE4) Inhibitor**

- ensifentrine (Ohtuvayre)

COPD Agents

- It is estimated that 16.4 million people have a COPD diagnosis in the U.S.
- It is characterized by the presence of airflow obstruction due to chronic bronchitis or emphysema
- Airflow obstruction is generally progressive, may be accompanied by airway hyperreactivity, and may be partially reversible
- 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
- Exacerbations and comorbidities contribute to the overall severity in individual patients
- COPD continues to be a leading cause of chronic morbidity and mortality worldwide

COPD Agents

- Both chronic bronchitis and emphysema predispose patients to a common collection of symptoms and impairments in respiratory function
- These include reductions in forced expiratory volume in one second (FEV1), forced vital capacity (FVC), FEV1/FVC ratio, and forced expiratory flow
- A COPD exacerbation is defined as an acute event characterized by worsening of the patient's respiratory symptoms that varies from the normal daily variations and requires a change in medication
- Patients are classified separately by both their GOLD severity and exacerbation/symptom assessment

COPD Agents

2025 GOLD Guidelines	
Assessment of Airflow Limitation	
Gold 1	Mild, FEV1 ≥ 80% predicted
Gold 2	Moderate, FEV1 50% to 79% predicted
Gold 3	Severe, FEV1 30% to 49% predicted
Gold 4	Very severe, FEV1 < 30% predicted

COPD Agents

2025 GOLD Guidelines	
Assessment of Exacerbation Risk and Symptoms	
Patient Group A	0 or 1 moderate exacerbation per year (not leading to hospitalization); and CAT score < 10 or mMRC grade 0 to 1
Patient Group B	0 or 1 moderate exacerbation per year (not leading to hospitalization); and CAT score ≥ 10 or mMRC grade ≥ 2
Patient Group E	≥ 2 moderate exacerbations per year or ≥ 1 exacerbation leading to hospitalization; any CAT score or mMRC grade

COPD Agents

GOLD Guidelines Group A:

- Short-acting inhaled bronchodilator used on an as-needed basis is recommended as first choice while a long-acting beta2-agonist (LABA) or anticholinergic and the combination of short-acting inhaled beta2-agonist (SABA) and short-acting anticholinergic are considered as alternatives

GOLD Guidelines Group B:

- Patients in Group B should be initiated on a LABA/LAMA combination

GOLD Guidelines Group E:

- Patients in Group E should be initiated on a LABA/LAMA combination; triple therapy with Inhaled Corticosteroids (ICS)/LAMA/LABA can be considered for patients with eosinophils ≥ 300 cells/µL

COPD Agents

- Per the 2020 ATS guidelines for the pharmacologic management of COPD, treatment should be initiated with dual bronchodilators
- Escalation to triple therapy is recommended for persistent symptoms and exacerbations
- ICS use should be tailored based on exacerbation history and eosinophil level
- Discontinuation of ICS may be consideration if the patient's condition is stable

COPD Agents

- Bronchodilator medications are central to the symptomatic management of COPD
- They act to improve emptying of the lungs, reduce dynamic hyperinflation at rest and during exercise, and improve exercise performance
- They are given either as-needed or on a regular basis
- Regular treatment with long-acting bronchodilators is more effective and convenient than treatment with short-acting agents
- Combining bronchodilators of different pharmacological classes may improve efficacy and decrease the risk of side effects
- There is insufficient evidence to recommend one long-acting or antimuscarinic agent over another as therapy should be individualized

COPD Agents

Product/Guideline Update:

- FDA approved the first generic for Atrovent HFA (ipratropium bromide) inhalation aerosol

GI Motility, Chronic

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GI Motility, Chronic

Drug	Manufacturer	Indication(s)
alosetron (Lotronex®)	generic, Sebela	▪ Treatment of severe, diarrhea-predominant irritable bowel syndrome (IBS-D) in women who have chronic IBS symptoms and have failed conventional therapy
eluxadoline (Viberzi®)	Abbvie	▪ Treatment of irritable bowel syndrome with diarrhea (IBS-D) in adults
linaclotide (Linzess®)	Abbvie	▪ Treatment of chronic idiopathic constipation (CIC) in adults ▪ Treatment of irritable bowel syndrome with constipation (IBS-C) in adults ▪ Treatment of functional constipation (FC) in pediatric patients 6 to 17 years of age ▪ Treatment irritable bowel syndrome with constipation in pediatric patients 7 years of age and older
lubiprostone (Amitiza®)	generic, Takeda	▪ Treatment of chronic idiopathic constipation (CIC) in adults ▪ Treatment of irritable bowel syndrome with constipation (IBS-C) in females ≥ 18 years old ▪ Treatment of opioid-induced constipation (OIC) in adults with chronic, non-cancer pain, including patients with chronic pain related to prior cancer or its treatment who do not require frequent (e.g., weekly) opioid dosage escalation

GI Motility, Chronic

Drug	Manufacturer	Indication(s)
methylnaltrexone (Relistor®)	Salix	▪ Treatment of opiate-induced constipation (OIC) in adults with advanced illness or pain caused by active cancer who require opioid dosage escalation for palliative care (injection only) ▪ Treatment of OIC in adults taking opioids for chronic non-cancer pain, including patients with chronic pain related to prior cancer or its treatment who do not require frequent (e.g., weekly) opioid dosage escalation (tablet and injection formulations)
naldemedine (Symproic®)	Collegium	▪ Treatment of opioid-induced constipation (OIC) in adults with chronic non-cancer pain, including patients with chronic pain related to prior cancer or its treatment who do not require frequent (e.g., weekly) opioid dosage escalation
naloxegol (Movantik®)	Redhill, Valinor	▪ Treatment of opioid-induced constipation (OIC) in adults with chronic non-cancer pain, including patients with chronic pain related to prior cancer or its treatment who do not require frequent (e.g., weekly) opioid dosage escalation
plecanatide (Trulance®)	Salix	▪ Treatment of chronic idiopathic constipation (CIC) in adults ▪ Treatment of irritable bowel syndrome with constipation (IBS-C) in adults
prucalopride (Motegrity®)	generic, Shire	▪ Treatment of chronic idiopathic constipation (CIC) in adults
tenapanor (Ibsrela®)	Ardelyx	▪ Treatment of irritable bowel syndrome with constipation (IBS-C) in adults

GI Motility, Chronic

- Chronic idiopathic constipation (CIC) is diagnosed if there are < 3 spontaneous bowel movements (SBMs) per week with symptoms occurring for ≥ 6 months
- Irritable bowel syndrome (IBS) is a functional bowel disorder which can be chronic, relapsing, and often lifelong
- IBS occurs in up to 15% of the population
- Patients present with a combination of symptoms that are typically constipation predominant (IBS-C), diarrhea predominant (IBS-D), alternating between both, or mixed (IBS-M)
- There are no comparative trials among these agents for their respective indications

GI Motility, Chronic

- Per the 2021 American College of Gastroenterology (ACG) guidelines for the management of IBS, for IBS-C:
  - Lubiprostone, linaclotide, and plecanatide are strongly recommended
  - Tenapanor was not addressed in this guideline

GI Motility, Chronic

- Per the 2022 American Gastroenterological Association (AGA) guidelines for the pharmacological management of IBS, for IBS-C:
  - Linaclotide is strongly recommended
  - Tenapanor, plecanatide, and lubiprostone are conditionally recommended
  - Shared decision-making and cost considerations are emphasized
  - Combining pharmacologic therapy with dietary and behavioral strategies are also recommended
  - Mild IBS often improves with diet alone, while medications are typically for moderate to severe symptoms

GI Motility, Chronic

- Per the AGA/ACG 2023 joint clinical practice guideline for CIC:
  - First-line therapy includes fiber supplementation, especially for low dietary intake, with psyllium having the best evidence
  - Can be used alone for mild cases or combined with other treatments
  - PEG (polyethylene glycol) is strongly recommended and is effective long-term (>6 months)
  - Magnesium oxide is an additional OTC option (very low certainty)
  - If OTC treatments fail or are intolerable, linaclotide, plecanatide, and prucalopride are strongly recommended
  - Additional options include senna and lubiprostone (low certainty) and lactulose (very low certainty)
  - Stimulant laxatives are recommended for short-term (≤4 weeks) or rescue use

GI Motility, Chronic

- Per the 2024 American Society of Colon and Rectal Surgeons (ASCRS) guideline for the evaluation and management of constipation:
  - First-line intervention is to increase fiber and fluid intake
  - Next step is to use osmotic laxatives, which are effective and safe for chronic use
  - Second-line treatment is short-term use of stimulant laxatives
  - If symptoms persist, linaclotide or lubiprostone may be used
  - No recommendations for plecanatide, prucalopride, or tenapanor

GI Motility, Chronic

- Per the 2019 AGA guideline on the medical management of opioid-induced constipation (OIC) :
  - First-line therapy is traditional laxatives
  - For laxative-refractory OIC, recommendations include naldemedine (high-quality evidence), naloxegol (moderate-quality evidence), or methylnaltrexone (low-quality evidence)
  - No clear recommendation is made for intestinal secretagogues (e.g., lubiprostone) or 5-HT agonists [e.g., prucalopride])

GI Motility, Chronic

- Functional constipation (FC) is a common childhood issue with no underlying organic cause
- It affects about 3% of pediatric patients worldwide
- First-line therapy is PEG due to strong safety, tolerability, and efficacy
- Normal fiber and fluid intake are recommended
- Additional options include stool softeners and short-term stimulant laxatives
- Linaclotide was approved in 2023 as the first prescription treatment for FC in children ages 6–17 years of age

Cytokine and CAM Antagonists

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Cytokine and CAM Antagonists

Drug	Manufacturer	Rheumatoid Arthritis (RA)	Juvenile Idiopathic Arthritis (JIA)	Ankylosing Spondylitis (AS)	Plaque Psoriasis (PSO)	Psoriatic Arthritis (PsA)	Crohn's Disease (CD)	Ulcerative Colitis (UC)	Other
Anti-Tumor Necrosis Factor (TNF) Biologics									
adalimumab (Humira®)	Abbvie Cordavis	X	X (≥ 2 years)	X	X	X	X (≥ 6 years)	X (≥ 5 years)	Hidradenitis suppurativa (HS) (ages ≥ 12 years) Uveitis (ages ≥ 2 years)
adalimumab-aacf Idacio®)	Fresenius Kabi	X	X (≥ 2 years)	X	X	X	X (≥ 6 years)	X (adults only)	HS adults only) Uveitis (adults only)
adalimumab-aaty (Yuflyma®)	Celltrion	X	X (≥ 2 years)	X	X	X	X (≥ 6 years)	X (adults only)	HS (adults only) Uveitis (adults only)
adalimumab-adaz (Hyrimoz®)	Sandoz Cordavis	X	X (≥ 2 years)	X	X	X	X (≥ 6 years)	X (adults only)	HS (adults only) Uveitis (adults only)
adalimumab-adbm (Cyltezo®)	Boehringer Ingelheim Quallent	X	X (≥ 2 years)	X	X	X	X (≥ 6 years)	X (adults only)	HS (adults only) Uveitis (adults only)
adalimumab-afzb (Abrilada™)	Pfizer	X	X (≥ 2 years)	X	X	X	X (≥ 6 years)	X (adults only)	HS adults only) Uveitis (adult only)

Cytokine and CAM Antagonists

Drug	Manufacturer	Rheumatoid Arthritis (RA)	Juvenile Idiopathic Arthritis (JIA)	Ankylosing Spondylitis (AS)	Plaque Psoriasis (PSO)	Psoriatic Arthritis (PsA)	Crohn's Disease (CD)	Ulcerative Colitis (UC)	Other
Anti-Tumor Necrosis Factor (TNF) Biologics									
adalimumab-aqvh (Yusimry™)	Coherus	X	X (≥ 2 years)	X	X	X	X (≥ 6 years)	X (adults only)	HS (adults only) Uveitis (adults only)
adalimumab-atto (Amjevita™)	Amgen Optum-Nuvaila	X	X (≥ 2 years)	X	X	X	X (≥ 6 years)	X (adults only)	HS (adults only) Uveitis (adults only)
adalimumab-bwwd (Hadlima™)	Organon	X	X (≥ 2 years)	X	X	X	X (≥ 6 years)	X (adults only)	HS (adults only) Uveitis (adults only)
adalimumab-fkjp (Hulio®)	Biocon Biologics;Mylan	X	X (≥ 2 years)	X	X	X	X (≥6 years)	X (adults only)	HS (adults only) Uveitis (adults only)
adalimumab-ryvk (Simlandi®)	Teva Quallent	X	X (≥ 2 years)	X	X	X	X (≥ 6 years)	X (adults only)	HS (adults only) Uveitis (adults only)

Cytokine and CAM Antagonists

Drug	Manufacturer	Rheumatoid Arthritis (RA)	Juvenile Idiopathic Arthritis (JIA)	Ankylosing Spondylitis (AS)	Plaque Psoriasis (PSO)	Psoriatic Arthritis (PsA)	Crohn's Disease (CD)	Ulcerative Colitis (UC)	Other
Anti-Tumor Necrosis Factor (TNF) Biologics									
certolizumab pegol (Cimzia®)	UCB	X	X (≥2 years)	X	X	X	X	--	Non-radiographic axial spondyloarthritis (nr-axSpA)
etanercept (Enbrel®)	Amgen	X	X (≥ 2 years)	X	X (≥ 4 years)	X (≥ 2 years)	--	--	--
golimumab SC (Simponi®)	Janssen Biotech	X	--	X	--	X	--	X	--
golimumab IV (Simponi® Aria®)	Janssen Biotech	X	X (≥ 2 years)	X	--	X (≥ 2 years)	--	--	--
infliximab (Remicade®)	generic, Janssen Biotech§	X	--	X	X	X	X (≥ 6 years)	X (≥ 6 years)	--
infliximab-abda (Renflexis®)	Merck/ Organon	X	--	X	X	X	X (≥ 6 years)	X (≥ 6 years)	--
infliximab-axxq (Avsola®)	Amgen	X	--	X	X	X	X (≥ 6 years)	X (≥ 6 years)	--
infliximab-dyyb (Inflectra®)	Pfizer	X	--	X	X	X	X (≥ 6 years)	X (≥ 6 years)	--
infliximab-dyyb (Zymfentra™)	Celltrion	--	--	--	--	--	X	X	--

Cytokine and CAM Antagonists

Drug	Manufacturer	Rheumatoid Arthritis (RA)	Juvenile Idiopathic Arthritis (JIA)	Ankylosing Spondylitis (AS)	Plaque Psoriasis (PSO)	Psoriatic Arthritis (PsA)	Crohn's Disease (CD)	Ulcerative Colitis (UC)	Other
Other Biologic Agents									
abatacept (Orencia®)	Bristol-Myers Squibb	X	X (≥ 6 years: IV) (≥ 2 years: SC)	--	--	X (≥ 2 years)	--	--	Graft versus Host Disease (GVHD)
anakinra (Kineret®)	Sobi-Swedish Orphan Biovitrum	X	--	--	--	--	--	--	Cryopyrin-Associated Periodic Syndromes (CAPS) Deficiency of Interleukin-1 Receptor Antagonist (DIRA)
bimekizumab-bkzx (Bimzelx®)	UCB Pharma	--	--	X	X	X	--	--	nr-axSpA, HS
brodalumab (Siliq®)	Bausch	--	--	--	X	--	--	--	--
canakinumab (Ilaris®)	Novartis	--	X Still's Disease and Systemic JIA (≥ 2 years)	--	--	--	--	--	Periodic Fever syndromes, including CAPS, TRAPS, HIDS, MKD, FMF
guselkumab (Tremfya®)	Janssen Biotech	--	--	--	X	X	X	X	--
inebilizumab-cdon (Uplizna®)	Horizon	--	--	--	--	--	--	--	Neuromyelitis optica spectrum disorder (NMOSD)
ixekizumab (Taltz®)	Eli Lilly	--	--	X	X (≥ 6 years)	X	--	--	nr-axSpA

Cytokine and CAM Antagonists

Drug	Manufacturer	Rheumatoid Arthritis (RA)	Juvenile Idiopathic Arthritis (JIA)	Ankylosing Spondylitis (AS)	Plaque Psoriasis (PSO)	Psoriatic Arthritis (PsA)	Crohn's Disease (CD)	Ulcerative Colitis (UC)	Other
Other Biologic Agents (continued)									
mirikizumab-mrkz (Omvoh®)	Eli Lilly	--	--	--	--	--	X	X	--
rilonacept (Arcalyst®)	Kiniksa	--	--	--	--	--	--	--	Periodic Fever syndromes: CAPS, FCAS, and MWS DIRA Recurrent pericarditis
risankizumab-rzaa (Skyrizi®)	Abbvie	--	--	--	X	X	X	X	--
sarilumab (Kevzara®)	Sanofi-Aventis	X	X	--	--	--	--	--	Polymyalgia rheumatica (PMR)
satralizumab-mwge (Enspryng®)	Genentech	--	--	--	--	--	--	--	NMOSD
secukinumab (Cosentyx®)	Novartis	--	--	X	X (≥ 6 years)	X (≥ 2 years)	--	--	nr-axSpA Enthesitis-related arthritis HS
spesolimab-sbzo (Spevigo®)	Boehringer Ingelheim	--	--	--	--	--	--	--	Generalized pustular psoriasis (GPP)
tildrakizumab-asmn (Ilumya®)	Sun	--	--	--	X	--	--	--	--
tocilizumab (Actemra®)	Genentech	X	X (≥ 2 years)	--	--	--	--	--	GCA SSc-ILD CRS

Cytokine and CAM Antagonists

Drug	Manufacturer	Rheumatoid Arthritis (RA)	Juvenile Idiopathic Arthritis (JIA)	Ankylosing Spondylitis (AS)	Plaque Psoriasis (PSO)	Psoriatic Arthritis (PsA)	Crohn's Disease (CD)	Ulcerative Colitis (UC)	Other
Other Biologic Agents (continued)									
tocilizumab-aazg (Tyenne®)	Fresenius Kabi	X	X (≥ 2 years)	--	--	--	--	--	GCA CRS (≥ 2 years)
tocilizumab-bavi (Tofidence™)	Biogen-Idec	X	X (≥ 2 years)	--	--	--	--	--	GCA
ustekinumab (Stelara®)	Janssen Biotech	--	--	--	X (≥ 6 years)	X (≥ 6 years)	X	X	--
ustekinumab-aauz (Otulfi™)	Fresinius Kabi	--	--	--	X (≥ 6 years)	X (≥ 6 years)	X	X	--
ustekinumab-aekn (Selarsdi™)	Teva	--	--	--	X (≥ 6 years)	X (≥ 6 years)	X	X	--
ustekinumab-auub (Wezlana)	Optum-Nuvaila	--	--	--	X (≥ 6 years)	X (≥ 6 years)	X	X	--
ustekinumab-kfce (Yesintek™)	Biocon Biologics	--	--	--	X (≥ 6 years)	X (≥ 6 years)	X	X	--
ustekinumab-stba (Steqeyma®)	Celltrion	--	--	--	X (≥ 6 years)	X (≥ 6 years)	X	X	--
ustekinumab-ttwe (Pyzchiva®)	Sandoz Quallent	--	--	--	X (≥ 6 years)	X (≥ 6 years)	X	X	--
vedolizumab (Entyvio®)	Takeda	--	--	--	--	--	X	X	--

Cytokine and CAM Antagonists

Drug	Manufacturer	Rheumatoid Arthritis (RA)	Juvenile Idiopathic Arthritis (JIA)	Ankylosing Spondylitis (AS)	Plaque Psoriasis (PSO)	Psoriatic Arthritis (PsA)	Crohn's Disease (CD)	Ulcerative Colitis (UC)	Other
Non-Biologic Agents									
abrocitinib (Cibinqo™)	Pfizer	--	--	--	--	--	--	--	Atopic dermatitis
apremilast (Otezla®)	Amgen/ Celgene	--	--	--	X (age ≥ 6 years)	X	--	--	Oral ulcers associated with Behçet's disease
baricitinib (Olumiant®)	Eli Lilly	X	--	--	--	--	--	--	Alopecia areata
deucravacitinib (Sotyktu™)	Bristol-Myers Squibb	--	--	--	X	--	--	--	--
Etrasimod (Velsipity™)	Pfizer	--	--	--	--	--	--	X	--
ritlecitinib (Litfulo™)	Pfizer	--	--	--	--	--	--	--	Alopecia areata
tofacitinib (Xeljanz®, Xeljanz XR)	Pfizer	X	X (≥ 2 years)	X	--	X	--	X	--
upadacitinib (Rinvoq®)	Abbvie	X	X (≥ 2 years)	X	--	X (age ≥ 2 years)	X	X	nr-axSpA Atopic dermatitis

Cytokine and CAM Antagonists

- Cytokines and cell adhesion molecules (CAMs) have indications for use in rheumatoid arthritis (RA), plaque psoriasis (PsO), psoriatic arthritis (PsA), Crohn's disease (CD), ankylosing spondylitis (AS), idiopathic Juvenile Arthritis (JIA), Adult-Onset Still's Disease (AOSD), nonradiographic axial spondylarthritis (nr-axSpA), Ulcerative Colitis (UC), as well as other medical conditions
- Axial spondyloarthritis (axSpA) is an inflammatory disease primarily affecting the spine
- It is divided into AS which is the radiographic form and nr-axSpA, with no clear radiographic damage but involves symptoms and inflammation

Cytokine and CAM Antagonists

- Treatment options for AS include:
  - TNF inhibitors (adalimumab, etanercept, infliximab, certolizumab, golimumab)
  - IL-17 inhibitors (secukinumab, ixekizumab, bimekizumab)
  - JAK inhibitors (tofacitinib, upadacitinib)
- Treatment for nr-axSpA includes bimekizumab, certolizumab, ixekizumab, secukinumab, and upadacitinib
- No TNF inhibitor is preferred over another
- TNF inhibitors are favored over etanercept in patients with recurrent eye inflammation (iritis) and with inflammatory bowel disease (IBD)

Cytokine and CAM Antagonists

- Multiple biologic therapies are approved for CD, including:
  - TNF inhibitors (adalimumab, certolizumab pegol, infliximab)
  - IL-23 inhibitors (guselkumab, risankizumab, mirikizumab)
  - IL-12/23 inhibitor (ustekinumab)
  - Integrin inhibitor: vedolizumab
- Infliximab is also used for closing fistulas (enterocutaneous and rectovaginal) and maintaining fistula closure
- Adalimumab is approved for children ≥6 years with inadequate response to conventional therapy and in adults who cannot tolerate or failed infliximab
- Certolizumab and vedolizumab are used after failure of conventional therapy
- Direct comparisons between these agents are limited and treatment recommendations are guided by professional societies such as the AGA and ACG

Cytokine and CAM Antagonists

- Approved treatments for JIA include abatacept, adalimumab, etanercept, IV golimumab, sarilumab, tocilizumab, canakinumab, tofacitinib, upadacitinib, and biosimilars
- Initial treatment should be NSAIDs, glucocorticoids, or anakinra
- If disease persists, therapy can be escalated to canakinumab, tocilizumab, methotrexate, leflunomide, or TNF inhibitors
- Biologics in this class are generally not first-line in non-systemic disease, but may be used after inadequate response
- AOSD is a rare inflammatory condition and is considered the adult counterpart of systemic JIA
- First-line agents include NSAIDs and antipyretics
- For systemic disease, corticosteroids or methotrexate are recommended
- Canakinumab is the only FDA-approved therapy for AOSD in the U.S.

Cytokine and CAM Antagonists

- A wide range of therapies are approved for PsO, including:
  - Biologics: TNF inhibitors (adalimumab, etanercept, infliximab), IL-17 inhibitors (bimekizumab, brodalumab, certolizumab, ixekizumab, secukinumab), IL-23 inhibitors (guselkumab, risankizumab, tildrakizumab), and IL-12/23 inhibitor (ustekinumab)
  - Non-biologic oral agents: apremilast, deucravacitinib
- Cytokine-targeting biologics (e.g., IL and TNF inhibitors) generally have similar effectiveness
- Some agents (e.g., ustekinumab, ixekizumab) have shown stronger outcomes compared to etanercept in moderate to severe disease
- The 2019 AAD/NPF guidelines recommend TNF inhibitors (adalimumab, etanercept, infliximab) for moderate to severe psoriasis, as well as apremilast, brodalumab, guselkumab, ixekizumab, secukinumab, tildrakizumab, and ustekinumab for moderate to severe PsO

Cytokine and CAM Antagonists

- Approved therapies for PsA include:
  - Biologics: TNF inhibitors (adalimumab, etanercept, infliximab, certolizumab, golimumab), IL-17 inhibitors (bimekizumab, ixekizumab, secukinumab), IL-23 inhibitors (guselkumab, risankizumab), IL-12/23 inhibitor (ustekinumab), as well as abatacept
  - Oral non-biologics: apremilast, tofacitinib, upadacitinib
- Mild to moderate disease is often managed initially with NSAIDs and/or intra-articular corticosteroid injections
- TNF inhibitors show comparable effectiveness (e.g., similar ACR20 response rates)
- Choice of therapy is individualized, with skin involvement severity as an important factor

Cytokine and CAM Antagonists

- The 2018 American College of Rheumatology (ACR) and the National Psoriasis Foundation (NPF) guideline recommendations emphasize a treat-to-target approach
- Preferred treatment sequence:
  - TNF inhibitors (first-line for most patients)
  - IL-17 inhibitors
  - IL-12/23 inhibitors
  - Abatacept
  - Tofacitinib
- Oral small molecules (e.g., apremilast, JAK inhibitors) play a variable role depending on patient history and response

Cytokine and CAM Antagonists

- Approved therapies for RA include:
  - Biologics: abatacept, TNF inhibitors (adalimumab, etanercept, infliximab, certolizumab, golimumab), IL-6 inhibitors (sarilumab, tocilizumab), and IL-1 inhibitor (anakinra)
  - Targeted synthetic (oral) agents: JAK inhibitors (baricitinib, tofacitinib, upadacitinib)
- Anakinra is less effective and more toxic compared to TNF inhibitors
- The ACR 2021 guideline emphasizes a treat-to-target strategy
- First-line preference is to methotrexate monotherapy
- For persistent moderate to severe disease, methotrexate should be initiated rather than immediate combination with biologics
- If treatment fails, switching to a different drug class is recommended (rather than another drug in the same class)

Cytokine and CAM Antagonists

- Approved therapies for UC include:
  - Biologics: TNF inhibitors (adalimumab, infliximab, golimumab), IL-23 inhibitors (guselkumab, mirikizumab), IL-12/23 inhibitor (ustekinumab), Integrin inhibitor (vedolizumab)
  - Oral agents: JAK inhibitors (tofacitinib, upadacitinib), S1P modulator (etrasimod)
- Infliximab is effective for inducing remission in moderate to severe, refractory UC
- Golimumab is used for adults with moderate to severe UC who fail or cannot tolerate conventional therapies
- Vedolizumab is typically used after failure or intolerance to TNF inhibitors, immunomodulators, or corticosteroids
- Treatment is guided by expert recommendations from the ACG and AGA

Cytokine and CAM Antagonists

- Transplant/Immunology: abatacept
- Hidradenitis Suppurativa (HS): adalimumab, bimekizumab
- Atopic Dermatitis: abrocitinib, upadacitinib
- Alopecia Areata: baricitinib, ritlecitinib
- Generalized Pustular Psoriasis flares: spesolimab
- Uveitis: adalimumab
- Behcet's disease (oral ulcers): apremilast
- Enthesitis-related arthritis (ERA): secukinumab
- CAPS (FCAS, MWS): canakinumab, rilonacept
- NOMID: anakinra
- DIRA: anakinra, rilonacept
- Recurrent pericarditis: rilonacept
- NMOSD (AQP4+): inebilizumab (IV), satralizumab (SC)
- GCA, CAR-T-cell–induced CRS, and SSc-ILD: tocilizumab

Cytokine and CAM Antagonists

Product/Guideline Updates:

- The FDA has approved a biosimilar to Stelara (ustekinumab), Steqeyma (ustekinumab-stba)
- The biosimilars Yesintek (ustekinumab-kfce) and Pyzchiva (ustekinumab-ttwe) were approved as interchangeable with Stelara (ustekinumab)
- Otulfi (ustekinumab-aauz) injection 45 mg/0.5 mL vial for SC use approved as interchangeable with Stelara (ustekinumab) injection 45 mg/0.5 mL vial for SC use
- Amjevita (adalimumab-atto): FDA approved the following presentations as interchangeable to corresponding Humira presentations: 80 mg/0.8 mL prefilled syringe and autoinjectors, the 20 mg/0.2mL prefilled syringes, and the 40 mg/0.4 mL autoinjector and PFS

Cytokine and CAM Antagonists

Product/Guideline Updates:

- FDA approved Tyenne (biosimilar to Actemra) for:
  - 1) Adults and pediatrics ≥ 2 years old with CAR-T-cell induced severe or life-threatening cytokine release syndrome (CRS)
  - (2) Hospitalized adults with COVID-19 who are receiving systemic corticosteroids and require supplemental oxygen, non-invasive or invasive mechanical ventilation, or extracorporeal membrane oxygenation (ECMO)
- Starjemza (ustekinumab-hmny) is an interchangeable biosimilar for Stelara
- The FDA approved an unbranded biosimilar 40 mg/0.4 mL prefilled syringe for SC use as interchangeable to the corresponding presentation of Humira

Cytokine and CAM Antagonists

Product/Guideline Updates:

- An unbranded biosimilar to Stelara (ustekinumab-stba) is now available as a 45 mg/0.5 mL solution in a single dose (SD) vial for SC use in pediatric patients aged 6 to 17 years weighing < 60 kg with PsO or PsA
- This new presentation is an interchangeable biosimilar to Stelara 45 mg/0.5 mL SDV for SC use
- FDA approved an unbranded version of Hadlima (adalimumab-bwwd) (biosimilar to Humira) for SC administration
- Approved as 40 mg/0.8 mL SD autoinjector, SD syringe and SDV (institutional use), and 40 mg/0.4 mL SD autoinjector and SD syringe
- FDA approved Dupixent (dupilumab) for treatment of adults with bullous pemphigoid (BP)
- Otezla (apremilast) indication for treatment of active PsA has been expanded to include pediatrics ≥ 6 years old weighing ≥ 20 kg

Cytokine and CAM Antagonists

Product/Guideline Updates:

- Avtozma (tocilizumab-anoh) is now approved for the treatment of patients ≥2 years with CAR-T cell-induced severe or life-threatening cytokine release syndrome (CRS)
- Actemra (tocilizumab) indication for treatment of COVID-19 in hospitalized patients who are receiving systemic corticosteroids and require supplemental oxygen, non-invasive or invasive mechanical ventilation, or ECMO has been expanded to include pediatrics ≥ 2 years old
- FDA approved apremilast extended-release tablets (Otezla XR) for treatment of adults with: (1) active PsA, (2) PSO who are candidates for phototherapy or systemic therapy, and (3) oral ulcers associated with Behcet's disease
- It is also approved for patients ≥ 6 years old and weighing ≥ 50 kg with: (1) active PsA or (2) moderate to severe PSO who are candidates for phototherapy or systemic therapy

Cytokine and CAM Antagonists

Product/Guideline Updates:

- Global consensus on the management of pregnancy in IBD was published in the American Journal of Gastroenterology
- Clinical guidelines regarding pharmacotherapy for the mother were included, as well as vaccination recommendations for children born to mothers with IBD
- Tremfya has received expanded indications for patients ≥ 6 years of age who weigh ≥ 40 kg with (1) moderate to severe plaque psoriasis and who are candidates for systemic therapy or phototherapy and (2) active psoriatic arthritis
- Indication for Simponi (golimumab) for UC has been expanded to include adults and pediatrics weighing ≥ 15 kg with moderately to severely active UC

Cytokine and CAM Antagonists

Product/Guideline Updates:

- Interchangeable biosimilars for Humira (Amjevita, Cyltezo, Hyrimoz, Simlandi and Yuflyma) are now approved to treat moderate to severe HS in patients ≥ 12 years
- They are also now approved for the treatment of non-infectious intermediate, posterior and panuveitis in patients ≥ 2 years
- Xeljanz and Xeljanz XR (tofacitinib) are now approved for the treatment of active PsA in patients who have had an inadequate response or intolerance to ≥ 1 TNF blocker in patients ≥ 2 years
- FDA approved inebilizumab-cdon (Uplizna) for treatment of generalized myasthenia gravis (gMG) in adults who are anti-acetylcholine receptor (AChR) or anti-muscle specific tyrosine kinase (MuSK) antibody positive

Cytokine and CAM Antagonists

Product/Guideline Updates:

- Idacio, a biosimilar to Humira (adalimumab), received label updates to expand indications of (1) uveitis (UV) to pediatrics patients ≥ 2 years old and (2) HS to patients ≥ 12 years old
- FDA approved deucravacitinib (Sotyktu) for treatment of adults with active PsA
- FDA approved icotrokinra (Icotyde) for the treatment of moderate to severe PsA in patients ≥ 12 years old who weigh ≥ 40 kg who are candidates for systemic therapy or phototherapy
- FDA approved Cosentyx SC for the treatment of moderate to severe HS in patients ≥ 12 years old

Glucagon Agents

Glucagon Agents

Class Overview: Products

- Diazoxide Suspension (Proglycem)
- Glucagon Injection (Glucagon Emergency Kit, Gvoke Syringe, Gvoke Vial)
- Dasiglucagon (Zegalogue Autoinjector, Zegalogue Syringe)
- Glucagon Nasal (Baqsimi)
- Glucagon Pen (Gvoke Pen)

Glucagon Agents

- Hypoglycemia is classified as:
  - Level 1 (glucose < 70 mg/dL and ≥ 54 mg/dL)
  - Level 2 (glucose < 54 mg/dL)
  - Level 3 (severe event: altered mental and/or physical status requiring assistance to treat)
- It can be reversed through administration of rapid-acting glucose or glucagon
- For patients unable or not willing to consume carbohydrates by mouth, use of glucagon is indicated for treating hypoglycemia
- The ADA 2026 Standards of Medical Care in Diabetes recommend glucagon should be prescribed for all individuals who are at an increased risk for level 2 or level 3 hypoglycemia to have accessible for use, as needed

Glucagon Agents

- Diazoxide is used in the management of hypoglycemia due to hyperinsulinism associated with the following conditions:
  - Inoperable islet cell adenoma or carcinoma, or extrapancreatic malignancy in adults
  - Leucine sensitivity, islet cell hyperplasia, nesidioblastosis, extrapancreatic malignancy, islet cell adenoma, or adenomatosis in infants and children
- It should be used only after a diagnosis of hypoglycemia due to one of the above conditions has been definitely established

Glucagon Agents

- Glucagon and dasiglucagon are indicated for the treatment of severe hypoglycemia in patients with diabetes
- Zegalogue, Baqsimi, and Gvoke offer the convenience of avoiding use of a powder that requires reconstitution to be administered
- All glucagon products are considered equally effective in reversing insulin-induced hypoglycemia
- Glucagon products that do not require reconstitution are now preferred by the ADA and the Endocrine Society because the easier administration allows for quicker correction of hypoglycemia

Growth Hormone

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Growth Hormone

Class Overview: Products

- Genotropin cartridge and syringe (somatropin)
- Humatrope cartridge and vial (somatropin)
- Ngenla (somatrogon-ghla)
- Norditropin pens (somatropin)
- Nutropin AQ NuSpin cartridge (somatropin)
- Omnitrope cartridge and vial (somatropin)
- Saizen cartridge and vials (somatropin)
- Serostim vials (somatropin)
- Skytrofa (lonapegsomatropin-tcgd)
- Sogroya (somapacitan-beco)
- Zomacton vials (somatropin)
- Zorbtive vials (somatropin)

Growth Hormone

- Growth hormone replacement products are similar in their clinical effects
- No head-to-head data are available, with the exception of lonapegsomatropin-tcgd (Skytrofa) compared to somatropin (Genotropin) for pediatric patients with growth hormone deficiency (GHD) (heiGHt study)
- Annualized height velocity (AHV) for lonapegsomatropin-tcgd was found to be non-inferior and superior to that observed with daily somatropin
- No pharmacologic difference among the agents exists in terms of safety and efficacy

Growth Hormone

- The 2019 American Association of Clinical Endocrinologists Clinical Practice guidelines indicated there is no evidence to support any specific product over another
- They recommend using individualized dose adjustments to improve effectiveness and to minimize side effects
- The primary indication for these products is GHD: Genotropin; Humatrope; Norditropin; Nutropin AQ; Omnitrope; Saizen; Zomacton
- Skytrofa is indicated for the treatment of pediatric patients ≥ 1 year old who weigh ≥ 11.5 kg and have growth failure due to inadequate secretion of endogenous growth hormone (GH)

Growth Hormone

- Several products carry an indication for Turner Syndrome: Genotropin; Humatrope; Norditropin; Nutropin AQ; Omnitrope; Zomacton
- Six products are indicated for Idiopathic Short Stature: Genotropin; Humatrope; Nutropin AQ; Omnitrope; Norditropin; Zomacton
- The following products are indicated for Small for Gestational Age: Genotropin; Humatrope; Norditropin; Omnitrope; Zomacton
- Genotropin, Omnitrope, and Norditropin are indicated for Prader-Willi Syndrome
- Humatrope is also indicated for Short Stature Homeobox Gene
- Serostim is indicated for HIV wasting or cachexia
- Zorbtive is indicated for Short Bowel Syndrome

Growth Hormone

Product/Guideline Updates:

- Novo Nordisk will discontinue manufacture of Norditropin inj 30 mg/3 mL Flexpro pen
- Norditropin 5 mg/1.5 mL, 10 mg/1.5 mL and 15 mg/1.5 mL Flexpro pens remain on the market
- Skytrofa is now also FDA approved for replacement of endogenous growth hormone in adults with GHD
- Labeling for all products indicated to treat growth failure and/or short stature disorders in pediatric patients has been updated to include information on risk of osteonecrosis associated with slipped capital femoral epiphysis and/or rapid growth in this population

Growth Hormone

Product/Guideline Updates:

- New indications for Sogroya: Treatment of pediatric patients ≥ 2.5 years of age with:
  - Short stature born small for gestational age (SGA) and with no catch-up growth by 2 years old
  - Growth failure associated with Noonan syndrome (NS)
  - Idiopathic Short Stature (ISS)

Hepatitis C Agents Direct Acting

ARIZONA HEALTH CARE COST CONTAINMENT SYSTEM

Hepatitis C Agents (Direct Acting)

Drug	Mfr	FDA-Approved Indications
Oral NS5B Polymerase Inhibitor		
sofosbuvir (Sovaldi®)	Gilead	Chronic hepatitis C genotype 1, 2, 3, or 4 in adults ▪ As a component of a combination antiviral treatment regimen ▪ Without cirrhosis or with compensated cirrhosis Chronic hepatitis C genotypes 2 or 3 in pediatric patients (≥ 3 years of age) ▪ In combination with ribavirin ▪ Without cirrhosis or with compensated cirrhosis
Oral Combination Products		
elbasvir/grazoprevir (Zepatier®)	Merck Sharpe & Dohme	Chronic hepatitis C genotype 1 or 4 in adult and pediatric patients ≥ 12 years of age or weighing ≥ 30 kg ▪ Co-formulated fixed-dose tablet of elbasvir (an NS5A inhibitor) and grazoprevir (an NS3/4A protease inhibitor) ▪ Indicated for use with or without ribavirin ▪ Testing for NS5A resistance-associated polymorphisms needed for genotype 1a ▪ Without cirrhosis or with compensated cirrhosis
glecaprevir/ pibrentasvir (Mavyret®)	AbbVie	Acute or chronic hepatitis C genotype 1, 2, 3, 4, 5, or 6 infection in adults and pediatric patients (≥ 3 years of age) ▪ Mavyret includes a combination of glecaprevir (an NS3/4A protease inhibitor) and pibrentasvir (an NS5A inhibitor) ▪ Indicated for use without ribavirin ▪ Without cirrhosis or with compensated cirrhosis Indicated for use in treatment-experienced genotype 1 in adults and pediatric patients (≥ 3 years of age) with prior regimen containing either an HCV NS5A inhibitor or an HCV NS3/4A PI, but not both

Hepatitis C Agents (Direct Acting)

Drug	Mfr	FDA-Approved Indications
Oral Combination Products (continued)		
ledipasvir/sofosbuvir (Harvoni®)	generic, Gilead	Chronic hepatitis C genotype 1, 4, 5, or 6 in adults and pediatric patients (≥ 3 years of age) ▪ Without cirrhosis or with compensated cirrhosis ▪ Co-formulated fixed-dose tablet of ledipasvir (an NS5A inhibitor) and sofosbuvir (an NS5B Inhibitor) ▪ Indicated for use without ribavirin Chronic hepatitis C genotype 1 in adults and pediatric patients (≥ 3 years of age) ▪ With decompensated cirrhosis, in combination with ribavirin ▪ Chronic hepatitis C genotypes 1 or 4 in adults and pediatric patients (≥ 3 years of age) who are liver transplant recipients without cirrhosis or with compensated cirrhosis, in combination with ribavirin
sofosbuvir/velpatasvir (Epclusa®)	generic*, Gilead	Chronic hepatitis C genotype 1, 2, 3, 4, 5, or 6 infection in adults and pediatric patients ≥ 3 years of age ▪ Epclusa includes a combination of sofosbuvir (an NS5B polymerase inhibitor) and velpatasvir (an NS5A inhibitor) ▪ Without cirrhosis or with compensated cirrhosis ▪ With decompensated cirrhosis, in combination with ribavirin Treatment-naïve or treatment-experienced liver transplant recipients without cirrhosis or with compensated cirrhosis
sofosbuvir/velpatasvir/ voxilaprevir (Vosevi®)	Gilead	Chronic hepatitis C genotype 1, 2, 3, 4, 5, or 6 infection in adults ▪ Vosevi includes a combination of sofosbuvir (an NS5B polymerase inhibitor), velpatasvir (an NS5A inhibitor), and voxilaprevir (an HCV NS3/4A protease inhibitor) ▪ Treatment-experienced genotype 1, 2, 3, 4, 5, and 6 patients with prior regimen containing an HCV NS5A inhibitor ▪ Treatment-experienced genotype 1a or 3 patients with prior regimen containing sofosbuvir without an NS5A inhibitor ▪ Indicated for use without ribavirin ▪ Without cirrhosis or with compensated cirrhosis Additional benefit over sofosbuvir/velpatasvir was not shown in adults with genotype 1b, 2, 4, 5, or 6 infection previously treated with sofosbuvir without a NS5A inhibitor

Hepatitis C Agents (Direct Acting)

- 2.4 to 3.9 million people in the U.S. are chronically infected
- The American Association for the Study of Liver Diseases (AASLD)/Infectious Diseases Society of America (IDSA) Recommendations for Testing, Managing, and Treating Hepatitis C recommend the use of different antiviral therapies based on the genotype identified and co-morbidities
- The guidelines also provide treatment recommendations for children, patients who have failed previous therapy (partial or null responders), patients co-infected with HIV, patients with renal impairment, patients with hepatic impairment, are pregnant, have known or suspected hepatocellular cancer, and patients who develop recurrent HCV post liver transplant

Hepatitis C Agents (Direct Acting)

- All of these clinical parameters help determine appropriate agent selection, likelihood of response, and treatment duration
- The guidelines define regimens that are recommended, alternative, and not recommended
- The guidelines also offer expanded options for patients not addressed in the current FDA labeling
- The joint guidelines from the AASLD/IDSA for the management of hepatitis C continue to be updated with the advent of new therapies and other developments in care

Hepatitis C Agents (Direct Acting)

Summary of the AASLD/IDSA HCV Guidance Recommendations

Grading System Used to Rate the Level of the Evidence and Strength of the Recommendation for Each Recommendation

- **Classification:**
  - **Class I –** Conditions for which there is evidence and/or general agreement that a given diagnostic evaluation, procedure, or treatment is beneficial, useful, and effective
  - **Class II –** Conditions for which there is conflicting evidence and/or a divergence of opinion about the usefulness and efficacy of a diagnostic evaluation, procedure, or treatment

Hepatitis C Agents (Direct Acting)

Summary of the AASLD/IDSA HCV Guidance Recommendations

Grading System Used to Rate the Level of the Evidence and Strength of the Recommendation for Each Recommendation

- **Classification (cont.):**
  - **Class IIa –** Weight of evidence and/or opinion is in favor of usefulness and efficacy
  - **Class IIb –** Usefulness and efficacy are less well established by evidence and/or opinion
  - **Class III –** Conditions for which there is evidence and/or general agreement that a diagnostic evaluation, procedure, or treatment is not useful and effective or if it in some cases may be harmful

Hepatitis C Agents (Direct Acting)

Summary of the AASLD/IDSA HCV Guidance Recommendations

Grading System Used to Rate the Level of the Evidence and Strength of the Recommendation for Each Recommendation

Level of Evidence:

- **Level A –** Data derived from multiple randomized clinical trials, meta-analyses, or equivalent
- **Level B –** Data derived from a single randomized trial, nonrandomized studies, or equivalent
- **Level C –** Consensus opinion of experts, case studies, or standard of care

Hepatitis C Agents (Direct Acting)

Treatment Experience	Treatment	Duration (weeks)	Rating
Any Genotype - Simplified Treatments			
Treatment-Naïve	Patients without cirrhosis: ▪ glecaprevir/pibrentasvir ▪ sofosbuvir/velpatasvir Patients with compensated cirrhosis: ▪ glecaprevir/pibrentasvir ▪ sofosbuvir/velpatasvir (all genotypes [GT] except GT 3 with Y93H present)	 8 12 8 12	 --
Any Genotype			
Treatment-Experienced **(previous sofosbuvir/ velpatasvir/ voxilaprevir treatment failure)**	Patients with or without compensated cirrhosis: ▪ glecaprevir/pibrentasvir + sofosbuvir + weight-based RBV ▪ sofosbuvir/velpatasvir/voxilaprevir + weight-based RBV	 16 24	 Class IIa, Level B Class IIa, Level B
Treatment-Experienced (previous failure of sofosbuvir-based regimen)	Patients without cirrhosis: ▪ sofosbuvir/velpatasvir/voxilaprevir Patients with compensated cirrhosis: ▪ sofosbuvir/velpatasvir/voxilaprevir (for genotype 3 and cirrhosis; add RBV)	 12 12	 Class I, Level A Class I, Level A
Treatment-Experienced (previous failure of elbasvir/grazoprevir)	Patients with or without cirrhosis: ▪ sofosbuvir/velpatasvir/voxilaprevir	 12	 Class I, Level A
Treatment-Experienced **(previous glecaprevir/ pibrentasvir treatment failure)**	Patients with or without compensated cirrhosis: ▪ glecaprevir/pibrentasvir + sofosbuvir + weight-based RBV ▪ sofosbuvir/velpatasvir/voxilaprevir ▪ sofosbuvir/velpatasvir/voxilaprevir + weight-based RBV (patients with compensated cirrhosis)	 16 12 12	 Class IIa, Level B Class IIa, Level B Class IIa, Level C
Any Genotype – Alternative Treatments			
Treatment-Experienced (previous failure of sofosbuvir-based regimen)	Patients with or without compensated cirrhosis: ▪ glecaprevir/pibrentasvir (except for NS3/4 PI inclusive combination DAA regimen failures; not for genotype 3 infection with sofosbuvir/NS5A inhibitor experience or for those with prior exposure to an NS5A inhibitor + NS3/4 PI regimen)	 16	 Class I, Level A

Hepatitis C Agents (Direct Acting)

Treatment Experience	Treatment	Duration (weeks)	Rating
Genotype 1a – Recommended Treatments			
Treatment-Naïve	Patients without cirrhosis:		
	▪ glecaprevir/pibrentasvir	8	Class I, Level A
	▪ ledipasvir/sofosbuvir	12	Class I, Level A
	▪ ledipasvir/sofosbuvir (HIV-uninfected and HCV RNA level < 6 million IU/mL)	8	Class I, Level B
	▪ sofosbuvir/velpatasvir	12	Class I, Level A
	Patients with compensated cirrhosis:		
	▪ ledipasvir/sofosbuvir	12	Class I, Level A
	▪ sofosbuvir/velpatasvir	12	Class I, Level A
	▪ glecaprevir/pibrentasvir	8	Class I, Level B
Genotype 1a – Alternative Treatments			
Treatment-Naïve	Patients with or without compensated cirrhosis:		
	▪ elbasvir/grazoprevir	12	Class I, Level A
Genotype 1b – Recommended Treatments			
Treatment-Naïve	Patients without cirrhosis:		
	▪ elbasvir/grazoprevir	12	Class I, Level A
	▪ glecaprevir/pibrentasvir	8	Class I, Level A
	▪ ledipasvir/sofosbuvir	12	Class I, Level A
	▪ ledipasvir/sofosbuvir (HIV-uninfected, and HCV RNA level < 6 million IU/mL)	8	Class I, Level B
	▪ sofosbuvir/velpatasvir	12	Class I, Level A
	Patients with compensated cirrhosis:		
	▪ elbasvir/grazoprevir	12	Class I, Level A
	▪ ledipasvir/sofosbuvir	12	Class I, Level A
	▪ sofosbuvir/velpatasvir	12	Class I, Level A
	▪ glecaprevir/pibrentasvir	8	Class I, Level B

Hepatitis C Agents (Direct Acting)

Treatment Experience	Treatment	Duration (weeks)	Rating
Genotype 2 – Recommended Treatments			
Treatment-Naïve	Patients without cirrhosis: ▪ glecaprevir/pibrentasvir ▪ sofosbuvir/velpatasvir Patients with compensated cirrhosis: ▪ sofosbuvir/velpatasvir ▪ glecaprevir/pibrentasvir	 8 12 12 8	 Class I, Level A Class I, Level A Class I, Level A Class I, Level B
Genotype 3 – Recommended Treatments			
Treatment-Naïve	Patients without cirrhosis: ▪ glecaprevir/pibrentasvir ▪ sofosbuvir/velpatasvir Patients with compensated cirrhosis: ▪ sofosbuvir/velpatasvir (without NS5A Y93H present) ▪ glecaprevir/pibrentasvir	 8 12 12 8	 Class I, Level A Class I, Level A Class I, Level A Class I, Level B
Genotype 3 – Alternative Treatments			
Treatment-Naïve	Patients with compensated cirrhosis: ▪ sofosbuvir/velpatasvir/voxilaprevir (when NS5A Y93H is present) ▪ sofosbuvir/velpatasvir ± weight-based RBV (when NS5A Y93H is present)	 12 12	 Class IIa, Level B Class IIa, Level A

Hepatitis C Agents (Direct Acting)

Treatment Experience	Treatment	Duration (weeks)	Rating
Genotype 4 – Recommended Treatments			
Treatment-Naïve	Patients without cirrhosis:		
	▪ glecaprevir/pibrentasvir	8	Class I, Level A
	▪ sofosbuvir/velpatasvir	12	Class I, Level A
	▪ ledipasvir/sofosbuvir	12	Class I, Level A
	▪ elbasvir/grazoprevir	12	Class I, Level A
	Patients with compensated cirrhosis:		
	▪ sofosbuvir/velpatasvir	12	Class I, Level A
	▪ glecaprevir/pibrentasvir (HIV/HCV-coinfected)	8 (12)	Class I, Level B
	▪ elbasvir/grazoprevir	12	Class IIa, Level B
	▪ ledipasvir/sofosbuvir	12	Class IIa, Level B
Genotype 5/6 – Recommended Treatments			
Treatment-Naïve	Patients without cirrhosis:		
	▪ glecaprevir/pibrentasvir	8	Class I, Level A
	▪ sofosbuvir/velpatasvir	12	Class I, Level B
	▪ ledipasvir/sofosbuvir (not recommended for genotype 6e)	12	Class IIa, Level B
	Patients with compensated cirrhosis:		
	▪ glecaprevir/pibrentasvir	8	Class I, Level B
	▪ sofosbuvir/velpatasvir	12	Class I, Level B
	▪ ledipasvir/sofosbuvir (not recommended for genotype 6e)	12	Class IIa, Level B

Hepatitis C Agents (Direct Acting)

Product/Guideline Updates:

- Zepatier 50 mg/100 mg tablets has been discontinued in December 2025

Hypoglycemics, Incretin Mimetics/Enhancers

ARIZONA HEALTH CARE COST CONTAINMENT SYSTEM

Hypoglycemics, Incretin Mimetics/Enhancers

Drug	Manufacturer	Indications
Amylin Analogue		
pramlintide (Symlin®)	AstraZeneca	▪ Adjunct therapy in type 1 and type 2 diabetes patients who use mealtime insulin therapy and have failed to achieve desired glucose control despite optimal insulin therapy (with or without concurrent sulfonylurea and/or metformin in type 2 patients)
Dipeptidyl Peptidase-4 (DPP-4) Enzyme Inhibitors		
alogliptin (Nesina®)	Takeda, Perrigo/Padagis	▪ Adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus (T2DM)
alogliptin/metformin (Kazano®)	Takeda, Perrigo/Padagis*	
alogliptin/pioglitazone (Oseni®)	Takeda, Perrigo/Padagis*	
linagliptin (Tradjenta®)	Boehringer Ingelheim	▪ Adjunct to diet and exercise to improve glycemic control in adults with T2DM
linagliptin/empagliflozin (Glyxambi®) linagliptin/empagliflozin/metformin ER (Trijardy® XR)	Boehringer Ingelheim	▪ Adjunct to diet and exercise to improve glycemic control in adults with T2DM ▪ Empagliflozin is indicated to reduce the risk of cardiovascular death in adults with T2DM and established cardiovascular disease (CVD)

Hypoglycemics, Incretin Mimetics/Enhancers

Drug	Manufacturer	Indications
linagliptin/metformin (Jentadueto®)	Boehringer Ingelheim	Adjunct to diet and exercise to improve glycemic control in adults with T2DM when treatment with both linagliptin and metformin is appropriate
linagliptin/metformin ER (Jentadueto® XR)		
saxagliptin (Onglyza®)	generic, AstraZeneca	Adjunct to diet and exercise to improve glycemic control in adults with T2DM
saxagliptin/dapagliflozin (Qtern®)	AstraZeneca	
saxagliptin/metformin ER (Kombiglyze® XR)	generic, AstraZeneca	Adjunct to diet and exercise to improve glycemic control in adults with T2DM when treatment with both saxagliptin and metformin is appropriate
sitagliptin (Januvia®)	Merck Sharp & Dohme	Adjunct to diet and exercise to improve glycemic control in adults with T2DM
sitagliptin (Zituvio™)	Zydus	
sitagliptin (Brynovin™)	Arbor	
sitagliptin/ertugliflozin (Steglujan™)	Merck Sharp & Dohme	Adjunct to diet and exercise to improve glycemic control in adults with T2DM when treatment with both ertugliflozin and sitagliptin is appropriate
sitagliptin/metformin (Janumet®)	Merck Sharp & Dohme	Adjunct to diet and exercise to improve glycemic control in adults with T2DM when treatment with sitagliptin and metformin is appropriate
sitagliptin/metformin (Zituvimet)	Zydus	
sitagliptin/metformin ER (Janumet XR®)	Merck Sharp & Dohme	Adjunct to diet and exercise to improve glycemic control in adults with T2DM when treatment with both sitagliptin and metformin ER is appropriate
sitagliptin/metformin ER (Zituvimet® XR)	Zydus	

Hypoglycemics, Incretin Mimetics/Enhancers

Drug	Manufacturer	Indications
Glucagon-like Peptide-1 Receptor Agonists (GLP-1RA)		
dulaglutide (Trulicity®)	Eli Lilly	▪ Adjunct to diet and exercise to improve glycemic control in adults and pediatric patients ≥ 10 years of age with T2DM ▪ Reduce the risk of major adverse cardiovascular events (MACE) in adults with T2DM who have established CVD or multiple cardiovascular risk factors
exenatide (Byetta®)	AstraZeneca	▪ Adjunct to diet and exercise to improve glycemic control in adults with T2DM who are taking metformin, a sulfonylurea, thiazolidinedione (TZD), or a combination of metformin and a sulfonylurea or TZD but have not achieved adequate glycemic control ▪ Add-on therapy to insulin glargine, with or without metformin and/or a TZD, in conjunction with diet and exercise for adults with T2DM who are not achieving adequate glycemic control on insulin glargine alone
exenatide ER (Bydureon®, Bydureon BCise®)	AstraZeneca	▪ Adjunct to diet and exercise to improve glycemic control in adults and pediatric patients ≥ 10 years of age with T2DM

Hypoglycemics, Incretin Mimetics/Enhancers

Drug	Manufacturer	Indications
liraglutide (Victoza®)	Generics, Novo Nordisk	▪ Adjunct to diet and exercise to improve glycemic control in adult and pediatric patients ≥ 10 years of age with T2DM ▪ Reduce the risk of major adverse cardiovascular events (MACE) in adults with T2DM and established cardiovascular disease (CVD)
liraglutide/insulin degludec (Xultophy®)	Novo Nordisk	▪ Adjunct to diet and exercise to improve glycemic control in adults with T2DM
lixisenatide/insulin glargine (Soliqua®)	Sanofi-Aventis	▪ Adjunct to diet and exercise to improve glycemic control in adults with type T2DM
semaglutide (Ozempic®)	Novo Nordisk	▪ Adjunct to diet and exercise to improve glycemic control in adults with T2DM ▪ To reduce the risk of MACE (cardiovascular death, non-fatal myocardial infarction, non-fatal stroke) in adults with T2DM and established CVD ▪ To reduce the risk of sustained estimated glomerular filtration rate (eGFR) decline, end stage kidney disease, and CVD in adults with T2DM and chronic kidney disease
semaglutide (Rybelsus®)	Novo Nordisk	▪ Adjunct to diet and exercise to improve glycemic control in adults with T2DM ▪ To reduce the risk of MACE in adults with T2DM who are at high risk for these events
Glucose-dependent Insulinotropic Polypeptide (GIP) Receptor Agonist/GLP-1RA		
tirzepatide (Mounjaro®)	Eli Lilly	▪ Adjunct to diet and exercise to improve glycemic control in adults and children ≥ 10 years old with T2DM

Hypoglycemics, Incretin Mimetics/Enhancers

- Over 38.4 million people in the U.S. have diabetes
- Type 2 diabetes (T2DM) accounts for over 95% of all diagnosed cases of diabetes
- The dipeptidyl peptidase-4 (DPP-4) inhibitors have modest glucose-lowering effects with HbA1c decrements of 0.5% to 1%
- These agents are weight-neutral and have a low hypoglycemia risk when used as monotherapy or in conjunction with metformin
- Clinical trials demonstrated the following reductions in HbA1c: dulaglutide by 0.7% to 1.6%, exenatide and liraglutide by 0.5% to 1.6%, injectable semaglutide by 1.4% to 1.5%, and oral semaglutide by 1.2% to 1.4%

Hypoglycemics, Incretin Mimetics/Enhancers

- In clinical trials, mean reductions in HbA1c from baseline ranged from 1.87% to 2.58% with tirzepatide
- The tirzepatide CV outcomes study SURPASS-CVOT compared tirzepatide to dulaglutide in patients with T2DM and increased CVD risk
- Data from the trial showed that tirzepatide was noninferior to dulaglutide with respect to a composite of death from cardiovascular causes, myocardial infarction, or stroke
- Diabetes treatment regimens should be individualized based on factors including the need for weight loss, risk of hypoglycemia, and patient preference

Hypoglycemics, Incretin Mimetics/Enhancers

- The 2026 ADA guidelines prefer medications with proven CV and renal benefit in patients with CV and/or renal disease, respectively
- In patients with Atherosclerotic Cardiovascular Disease (ASCVD), a GLP-1RA and/or SGLT2 inhibitor with proven CVD benefit is preferred
- In patients with obesity and HFpEF, dual GIP/GLP-1 RA may be considered
- In patients with CKD, use SGLT2 inhibitor or GLP-1 RA with renal benefit; GLP-1 RA is preferred in advanced CKD (eGFR <30)

Hypoglycemics, Incretin Mimetics/Enhancers

- Per the ADA, GLP-1 RAs, GIP/GLP-1 RAs, and SGLT2 inhibitors are preferred when increased body weight is a concern
- To minimize hypoglycemia, GLP-1 RAs, SGLT2 inhibitors, metformin, DPP-4 inhibitors, or TZDs may be considered
- GLP-1 RAs or dual GIP/GLP-1 RAs are also preferred when there is co-existing liver disease (MASLD/MASH)
- Liraglutide, semaglutide, and dulaglutide reduce CV events
- In most pediatric T2DM patients, the ADA recommends starting with metformin
- Escalation with insulin or GLP-1 RA (approved for ≥10 years old) and/or SGLT2 inhibitor (empagliflozin) may be used as needed to achieve target glycemic control

Hypoglycemics, Incretin Mimetics/Enhancers

- The 2023 AACE guidelines suggest that patients with ASCVD or who are at very high risk for ASCVD should be initiated on a GLP-1RA or SGLT2 inhibitor
- Patients with history of stroke or TIA should be initiated on a GLP-1RA or pioglitazone
- Patients with CKD should be prescribed a SGLT2 inhibitor or GLP-1RA
- For those who are overweight, obese, or at risk for hypoglycemia, a GLP-1RA, dual GIP/GLP-1 RA, or SGLT2 inhibitor is preferred
- When severe hyperglycemia exists, basal insulin ± prandial insulin or GLP-1RA or dual GIP/GLP-1 based therapy is preferred

Hypoglycemics, Incretin Mimetics/Enhancers

- In 2024, ACP published guidelines on newer pharmacologic treatments in adults with T2DM
- Key recommendations include:
  - Adding SGLT2 or GLP-1RA to metformin and lifestyle modifications in those with inadequate glycemic control
  - Using a GLP-1RA to reduce the risk for all-cause mortality, MACE, and stroke
- They also state that sulfonylureas and long-acting insulins are inferior to SGLT-2 inhibitors and GLP-1 agonists in reducing all-cause mortality and morbidity

Hypoglycemics, Incretin Mimetics/Enhancers

- The KDIGO 2022 guidelines on managing diabetes in CKD recommend first-line treatment with metformin or a SGLT2 inhibitor in most patients with an eGFR ≥ 30 or 20 mL/min/1.73 m^2, respectively
- Long-acting GLP-1 RA can be used as add-on therapy if glycemic targets are not met with metformin and SGLT2 inhibitor
- In 2023, The American Heart Association (AHA)/ACC published guidelines for diagnosis and management for chronic coronary disease (CCD)
- They recommend SGLT2 inhibitors and GLP-1RAs in select patients with CCD, including groups without diabetes

Hypoglycemics, Incretin Mimetics/Enhancers

- The Center for Disease Control (CDC) estimates that up to 70% of patients with T2DM have MASLD and about 20–30% of those progress to MASH
- Per the 2025 AGA, GLP-1 RAs are preferred for patients with T2DM and/or obesity who have MASH
- Pioglitazone, SGLT2 inhibitors, and DPP-4 inhibitors are not specifically recommended for MASH treatment, but may still be used for glycemic control in T2DM patients with MASH

Hypoglycemics, Incretin Mimetics/Enhancers

- Per the 2022 ADA and the EASD position statement on the management of T2DM, all patients with T2DM, CVD, and CKD should be prescribed a SGLT2 inhibitor or GLP-1RA with proven benefit
- When T2DM is not adequately controlled with lifestyle management and metformin, a SGLT2 inhibitor or GLP-1RA is recommended when weight loss is a priority
- A DPP-4 inhibitor, GLP-1RA, SGLT2 inhibitor, or TZD is recommended when there is a compelling need to minimize hypoglycemia

Hypoglycemics, Incretin Mimetics/Enhancers

Product/Guideline Updates:

- Labeling has been updated to change the trade name of Rybelsus R2 formulation to Ozempic tablets
- Rybelsus tablets are available in 3 mg, 7 mg and 14 mg strengths; Ozempic tablets are available in 1.5 mg, 4 mg and 9 mg strengths
- Beginning May 4, 2026, Ozempic tablets (1.5 mg, 4 mg, 9 mg) will be available in the U.S.
- FDA approved the first generic for Qtern (dapagliflozin/saxagliptin) 10 mg/5 mg oral tablets

Immunologics (Immunomodulators, Atopic Dermatitis and Immunomodulators, Asthma)

ARIZONA HEALTH CARE COST CONTAINMENT SYSTEM

Immunomodulators, Atopic Dermatitis

Drug	Manufacturer	Indications
abrocitinib (Cibinqo®)	Pfizer	Treatment of refractory, moderate to severe atopic dermatitis in patients ≥ 12 years of age whose disease is not adequately controlled with other systemic drugs, including biologics, or when use of those therapies is inadvisable
crisaborole (Eucrisa®)	Pfizer	Treatment of mild to moderate atopic dermatitis in adult and pediatric patients ≥ 3 months of age
Delgocitinib (Anzupgo)	Leo Pharma	Treatment of moderate to severe chronic hand eczema (CHE) in adults who have had an inadequate response to, or for whom topical corticosteroids are inadvisable
dupilumab (Dupixent®)	Sanofi-Aventis	Treatment of patients ≥ 6 months of age 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
lebrikizumab-lbkz (Ebglyss)	Eli Lilly	Treatment of patients ≥ 12 years of age who weigh ≥ 40 kg 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
nemolizumab-ilto (Nemluvio)	Galderma	Treatment of patients ≥ 12 years of age with moderate-to-severe atopic dermatitis in combination with topical corticosteroids and/or calcineurin inhibitors when the disease is not adequately controlled with topical prescription therapies
pimecrolimus (Elidel®)	generic, Bausch	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, who have failed to respond adequately to other topical prescription treatments, or when those treatments are not advisable

Immunomodulators, Atopic Dermatitis

Drug	Manufacturer	Indications
roflumilast (Zoryve®)	Arcutis	Topical treatment of mild to moderate atopic dermatitis in adult and pediatric patients 2-5 years of age and ≥ 6 years old
ruxolitinib (Opzelura™)	Incyte	Topical short-term and non-continuous chronic treatment of mild to moderate atopic dermatitis in non-immunocompromised patients ≥ 2 years of age whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable
tacrolimus (Protopic®)	generic, Leo	Second-line therapy for the short-term and non-continuous chronic treatment of moderate to severe atopic dermatitis in non-immunocompromised adults and children 2 - 15 years of age who have failed to respond adequately to other topical prescription treatments for atopic dermatitis, or when those treatments are not advisable
tapinarof (Vtama®)#	Dermavant	Topical treatment of atopic dermatitis in adults and pediatric patients ≥ 2 years of age
tralokinumab-ldrm (Adbry®)	Leo	Treatment of moderate to severe atopic dermatitis in patients ≥ 12 years of age whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable; can be used with or without topical corticosteroids
upadacitinib (Rinvoq®)	AbbVie	Treatment of refractory, moderate to severe atopic dermatitis in patients ≥ 12 years of age whose disease is not adequately controlled with other systemic drugs, including biologics, or when use of those therapies is inadvisable

Immunomodulators, Atopic Dermatitis

- Atopic dermatitis (AD) is a chronic, non-contagious, inflammatory disease of the skin resulting from a combination of genetic and environmental factors
- Approximately 70% of patients diagnosed with AD have a positive family history of atopic diseases
- AD affects ~ 13% of children and ~ 7.3% of adults in the U.S.
- 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
- AD is characterized by extremely dry, itchy skin on the insides of the elbows, behind the knees, and on the face, hands, and feet
- Evidence suggests that patients with asthma or food allergies have an increased severity of AD
- There are also associations between AD and allergic rhinitis, anxiety, depression, heart disease, osteoporosis, and obesity

Immunomodulators, Atopic Dermatitis

The 2023 American Academy of Dermatology (AAD) Guidelines:

- Strongly recommend moisturizers, topical corticosteroids, topical calcineurin inhibitors, topical phosphodiesterase 4 (PDE-4) inhibitors, and topical JAK inhibitors for the treatment of AD
- Topical corticosteroids (TCS) are typically used first line for mild to severe dermatitis
- Topical calcineurin inhibitors are a safe anti-inflammatory option, especially when corticosteroid avoidance is warranted
- The guidelines note that tacrolimus might be more clinically effective than pimecrolimus, based on clinical trials

Immunomodulators, Atopic Dermatitis

- For mild to moderate disease, crisaborole has a favorable safety profile
- Topical ruxolitinib cream has demonstrated significant efficacy for short-term, non-continuous treatment of mild to moderate AD
- The guidelines note that the strong recommendation for JAK inhibitors in AD is based on moderate certainty, short-term efficacy and safety data
- Phototherapy is recommended as a treatment option after failure of emollients, TCS, and topical calcineurin inhibitors
- Systemic immunomodulators should be reserved for patients with inadequate responses to topical regimens and/or phototherapy

Immunomodulators, Atopic Dermatitis

- Dupilumab and tralokinumab are both strongly recommended for patients with moderate to severe AD
- Abrocitinib and upadacitinib are options typically after failure of other systemic therapies or when those aren't appropriate
- Topicals can be used alongside phototherapy or systemic agents for maintenance or flare control
- In 2025, the AAD released a Focused Update for AD
- This addresses four new FDA-approved therapies that are not covered in prior guidelines
- For mild–moderate AD in adults, roflumilast 0.15% cream (Zoryve) is strongly recommended
- For moderate to severe AD in adults, tapinarof cream (Vtama), lebrikizumab (Ebglyss), and nemolizumab (Nemluvio) are strongly recommended

Immunomodulators, Atopic Dermatitis

- The American Academy of Allergy, Asthma, and Immunology (AAAAI)/American College of Allergy, Asthma and Immunology (ACAAI) Joint Task Force published guidelines in 2023 for AD
- They recommend regular use of bland moisturizers as baseline therapy, which is essential before adding other treatments
- TCS can be added for patients not controlled on moisturizers
- Topical calcineurin inhibitors can be added for patients ≥3 months with inadequate control
- Crisaborole (high certainty) and topical ruxolitinib (low certainty) may be added for mild–moderate AD refractory to moisturizers
- Dupilumab (≥6 months) and tralokinumab (≥12 years) are strongly recommended for moderate to severe refractory AD when patients cannot tolerate or use mid/high-potency TCS
- Abrocitinib, baricitinib (off-label), and upadacitinib may be used in moderate–severe refractory AD after failure or intolerance to topicals and biologics

Immunomodulators, Atopic Dermatitis

Product/Guideline Updates:

- FDA has approved difamilast (Adquey) for the topical treatment of adults and pediatric patients ≥ 2 years of age with mild to moderate atopic dermatitis
- AAP updated recommendations on treating eczema; they recommend:
  - Use of moisturizer creams; ointments are alternative
  - Avoid triggers and contact allergens
  - Use of TCS to appropriately control chronic disease
  - “Proactive” treatment with topical anti-inflammatories to reduce flares of recurrent AD
  - Systemic treatment can be used when topicals are not adequate

Immunomodulators, Asthma

Drug	Manufacturer	Indications
Interleukin-5 (IL-5) Antagonists		
benralizumab (Fasenra®)	AstraZeneca	▪ Add-on maintenance treatment of patients aged 6 years and older with severe asthma, and with an eosinophilic phenotype ▪ Treatment of adults with eosinophilic granulomatosis with polyangiitis (EGPA)
depemokimab-ulaa (Exdensur)	GlaxoSmithKline	▪ Add-on maintenance treatment of severe asthma with an eosinophilic phenotype in patients ≥ 12 years
mepolizumab (Nucala®)	GlaxoSmithKline	▪ Add-on maintenance treatment of severe asthma in adults and pediatric patients aged ≥ 6 years with an eosinophilic phenotype ▪ Treatment of adult patients with eosinophilic granulomatosis with polyangiitis (EGPA)
reslizumab (Cinqair®)	Teva Specialty	▪ Add-on maintenance treatment of severe asthma in patients aged ≥ 18 years with an eosinophilic phenotype

Immunomodulators, Asthma

Drug	Manufacturer	Indications
Anti-Immune Globulin E (IgE) Antibody		
omalizumab (Xolair®)	Genentech	▪ 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
Thymic Stromal Lymphopoietin (TSLP) Blocker		
tezepelumab-ekko (Tezspire®)	Amgen	▪ Add-on maintenance treatment of severe asthma in adults and pediatric patients ≥ 12 years of age
Interleukin-4 (IL-4) Antagonist		
dupilumab (Dupixent®)	Regeneron/Sanofi-Aventis	▪ Add-on maintenance treatment in patients with moderate-to-severe asthma aged ≥ 6 years with an eosinophilic phenotype or with oral corticosteroid-dependent asthma

Immunomodulators, Asthma

- An estimated 8.9% of adults and 6.7% of children have asthma in the U.S.
- Asthma is typically characterized by chronic airway inflammation and hyperresponsiveness
- It is diagnosed based on history of respiratory symptoms and evidence of variable expiratory airflow limitation
- Type 2 inflammation is present in most individuals with severe asthma
- It is characterized by the presence of cytokines and elevation of eosinophils or fractional concentration of exhaled nitric oxide (FeNO)
- Generally, patients with eosinophilic asthma have severe disease with high eosinophil levels in the blood and sputum

Immunomodulators, Asthma

- The 2020 ATS and European Respiratory Society (ERS) Task Force Guidelines define severe asthma as requiring high-dose ICS plus another controller and/or systemic steroids to remain controlled, or remains uncontrolled despite this treatment
- IL-5–targeted therapies are recommended as add-on therapy for adults with severe uncontrolled asthma with an eosinophilic phenotype or those with severe corticosteroid-dependent asthma
- IL-5 or IL-5R agents may be initiated when blood eosinophils ≥150 cells/uL
- For allergic asthma (≥12 years), higher likelihood of response to omalizumab is with eosinophils ≥260 cells/uL or FeNO ≥19.5 ppb
- Dupilumab is suggested for severe eosinophilic or steroid-dependent asthma, regardless of eosinophil levels

Immunomodulators, Asthma

The 2025 Global Initiative for Asthma (GINA) Guideline:

- They use a stepwise approach
  - Mild asthma: Steps 1 and 2
  - Moderate asthma: Steps 3 and 4
  - Severe asthma: Step 5 (uncontrolled despite use of, or requiring, high-dose ICS-LABA
- Step 5 patients should be referred to a specialist for evaluation and phenotype assessment
- Add-on options for severe asthma patients include LAMA, azithromycin (off-label), leukotriene receptor antagonist (LTRA), and biologics (anti-IgE, anti-IL-5, anti-IL-4, anti-TSLP)
- Oral corticosteroids (OCS) should only be used as a last resort

Immunomodulators, Asthma

The 2025 Global Initiative for Asthma (GINA) Guideline (Cont.):

- Biologic therapies (Evidence A) for severe disease:
  - Omalizumab (anti-IgE): ≥6 years, allergic asthma
  - Anti-IL-5 agents: benralizumab (≥6), mepolizumab (≥6), reslizumab (≥18)
  - Dupilumab (anti-IL-4): ≥6 years, eosinophilic/Type 2 or OCS-dependent asthma
  - Tezepelumab (anti-TSLP): ≥12 years, severe asthma

Movement Disorders

ARIZONA
HEALTH CARE COST
CONTAINMENT SYSTEM

Movement Disorders

Drug	Manufacturer	Indication(s)
deutetrabenazine (Austedo, Austedo® XR)	Teva	Treatment of chorea associated with Huntington's disease Treatment of tardive dyskinesia
tetrabenazine (Xenazine)	generic, Lundbeck	Treatment of chorea associated with Huntington's disease
valbenazine (Ingrezza, Ingrezza® Sprinkle)	Neurocrine Biosciences	Treatment of chorea associated with Huntington's disease Treatment of tardive dyskinesia

Movement Disorders

- There are various types of movement disorders, including parkinsonism, tremor, dystonia, dyskinesia, tics, chorea, and other involuntary movements
- Chorea is a characteristic feature of Huntington's disease (HD)
- It affects approximately 90% of people with HD (over 35,000 people in the U.S.)
- The 2012 American Academy of Neurology (AAN) guidelines, that were retired in 2022, recommend tetrabenazine, amantadine, or riluzole for chorea associated with HD
- Deutetrabenazine has not been addressed in these clinical practice guidelines
- Deutetrabenazine, tetrabenazine, and valbenazine have demonstrated superiority over placebo for HD-associated chorea but have not been compared head-to-head in controlled trials

Movement Disorders

- In 2022, the International Parkinson and Movement Disorder Society (MDS) published evidence-based review on treatments for HD
- It was found that both deutetrabenazine and tetrabenazine are likely efficacious for chorea
- They concluded that deutetrabenazine is likely efficacious for motor impairment, while tetrabenazine is unlikely efficacious
- Deutetrabenazine is also likely efficacious for dystonia, but data were too limited regarding tetrabenazine
- Deutetrabenazine and tetrabenazine were determined unlikely efficacious in functional capacity improvement as well as gait and balance
- Both agents are only approved for the treatment of chorea associated with HD
- They categorized deutetrabenazine as unlikely harmful while tetrabenazine was considered likely harmful

Movement Disorders

- Tardive dyskinesia (TD) consists of involuntary movements of the tongue, lips, face, trunk, and extremities
- It generally occurs after long-term treatment with dopamine antagonists
- Happens at a rate of approximately 4% to 8% per year in adult patients treated with a first generation antipsychotics, which appears to be about 3 times the rate that has been observed with second generation antipsychotics
- In 2020, the American Psychiatric Association (APA) updated their guidelines for the treatment of schizophrenia

Movement Disorders

- They recommend that patients who have moderate to severe or disabling TD related to antipsychotic therapy be treated with deutetrabenazine, tetrabenazine, or valbenazine
- Patients with mild TD can also be considered for treatment with a VMAT2 inhibitor following an assessment of several factors
- They state that deutetrabenazine or valbenazine is preferred over tetrabenazine
- valbenazine and deutetrabenazin have demonstrated superiority over placebo in key clinical trials, but they have not been compared to each other or to other treatment strategies for TD

Multiple Sclerosis Agents

ARIZONA
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Multiple Sclerosis Agents

Drug	Manufacturer	Indication(s)
alemtuzumab (Lemtrada®)	Genzyme	▪ Relapsing forms of multiple sclerosis (MS), to include relapsing-remitting disease and active secondary progressive disease, in adults Due to its safety profile, the use of alemtuzumab should generally be reserved for patients who have had an inadequate response to ≥ 2 drugs indicated for the treatment of MS Due to its safety profile, alemtuzumab is not recommended for patients with clinically isolated syndrome (CIS)
cladribine (Mavenclad®)	EMD Serono	▪ Relapsing forms of MS, to include relapsing-remitting disease and active secondary progressive disease, in adults Due to its safety profile, the use of cladribine should generally be reserved for patients who have had an inadequate response to or are unable to tolerate an alternate drug indicated to treat MS Due to its safety profile, cladribine is not recommended for patients with CIS
dalfampridine (Ampyra®)	generic, Acorda	▪ Improve walking in patients with MS, demonstrated by an increase in walking speed
dimethyl fumarate (Tecfidera®)	generic, Biogen-Idec	▪ Relapsing forms of MS, to include CIS, relapsing-remitting disease, and active secondary progressive disease, in adults
diroximel fumarate (Vumerity®)	Biogen-Idec	▪ Relapsing forms of MS, to include CIS, relapsing-remitting disease, and active secondary progressive disease, in adults
fingolimod (Gilenya®)	generic, Novartis	▪ Relapsing forms of MS, to include CIS, relapsing-remitting disease, and active secondary progressive disease, in patients ≥ 10 years of age

Multiple Sclerosis Agents

Drug	Manufacturer	Indication(s)
fingolimod (Tascenso ODT®)	Cycle	▪ Relapsing forms of MS, to include CIS, relapsing-remitting disease, and active secondary progressive disease, in patients ≥ 10 years of age
glatiramer acetate (Copaxone®)	generic, Teva Neurosciences	▪ Relapsing forms of MS, to include CIS, relapsing-remitting disease, and active secondary progressive disease, in adults
interferon ß-1a IM (Avonex®)	Biogen-Idec	▪ Relapsing forms of MS, to include CIS, relapsing-remitting disease, and active secondary progressive disease, in adults
interferon ß-1a SC (Rebif®)	EMD Serono	
interferon ß-1a SC/IM (pegylated) (Plegridy®)	Biogen-Idec	▪ Relapsing forms of MS, to include CIS, relapsing-remitting disease, and active secondary progressive disease, in adults
interferon ß-1b (Betaseron®)	Bayer	▪ Relapsing forms of MS, to include CIS, relapsing-remitting disease, and active secondary progressive disease, in adults
interferon ß-1b (Extavia®)	Novartis	
monomethyl fumarate (Bafiertam®)	Banner Life Sciences	▪ Relapsing forms of MS, to include CIS, relapsing-remitting disease, and active secondary progressive disease, in adults

Multiple Sclerosis Agents

Drug	Manufacturer	Indication(s)
natalizumab (Tysabri®) natalizumab-sztn (Tyruko)	Biogen-Idec Sandoz	▪ Relapsing forms of MS, to include CIS, relapsing-remitting disease, and active secondary progressive disease, in adults† ▪ Inducing and maintaining clinical response and remission in adult patients with moderately to severely active Crohn's disease (CD) with evidence of inflammation who have had an inadequate response to, or are unable to tolerate, conventional CD therapies, including other biologic agents
ocrelizumab (Ocrevus®) Ocrelizumab/hyaluronidase -ocsq (Ocrevus Zunovo)	Genentech	▪ Relapsing MS, to include CIS, relapsing-remitting disease, and active secondary progressive disease, in adults ▪ Primary progressive multiple sclerosis (PPMS) in adults
ofatumumab (Kesimpta®)	Novartis	▪ Relapsing forms of MS, to include CIS, relapsing-remitting disease, and active secondary progressive disease, in adults
ozanimod (Zeposia®)	Celgene	▪ Relapsing form of MS, to include CIS, relapsing-remitting disease, and active secondary progressive disease, in adults ▪ Moderately to severely active ulcerative colitis (UC) in adults
ponesimod (Ponvory®)	Janssen	▪ Relapsing forms of MS, to include CIS, relapsing-remitting disease, and active secondary progressive disease, in adults
siponimod (Mayzent®)	Novartis	▪ Relapsing forms of MS, to include CIS, relapsing-remitting disease, and active secondary progressive disease, in adults
teriflunomide (Aubagio®)	generic, Sanofi-Aventis	▪ Relapsing forms of MS, to include CIS, relapsing-remitting disease, and active secondary progressive disease, in adults
ublituximab-xiiy (Briumvi®)	TG Therapeutics	▪ Relapsing forms of MS, to include CIS, relapsing-remitting disease, and active secondary progressive disease, in adults

Multiple Sclerosis Agents

- It is estimated that nearly 1 million people are living with Multiple sclerosis (MS) in the U.S.
- It is a complex human autoimmune-type inflammatory disease of the central nervous system (CNS)
- The nerve degeneration associated with MS can result in a wide variety of symptoms, including sensory disturbances in the limbs (e.g., numbness, paresthesia, burning, pain), optic nerve dysfunction, ataxia, fatigue, and bladder, bowel, and sexual dysfunction
- MS results in significant physical disability in over 30% of patients within 20 to 25 years of onset
- Cognitive dysfunction occurs in an estimated 40% to 70% of MS patients

Multiple Sclerosis Agents

- The clinical course of MS falls into one of the following categories:
  - Clinically isolated syndromes (CIS): the first episode of neurologic symptoms due to inflammation or demyelination lasting at least 24 hours
  - Relapsing-remitting MS (RRMS): clearly defined, self-limited attacks of neurologic dysfunction, followed by periods of remission without disease progression
  - Primary progressive MS (PPMS): nearly continuous worsening of disease not interrupted by distinct relapses
  - Secondary progressive MS (SPMS): Relapsing-remitting disease course at onset, followed by progression with or without occasional relapses, minor remissions, and plateaus

Multiple Sclerosis Agents

- According to the AAN, disease-modifying therapy (DMT) should be offered to people with relapsing forms of MS with recent clinical relapses or MRI activity or those with a single clinical demyelinating event and ≥ 2 brain lesions characteristic of MS if desired
- Treatments are intended to reduce relapses and new MRI lesion activity; they are not intended for symptom improvement
- Specific medications are recommended based on disease activity, treatment access, and adverse effect profiles
- It is typically recommended that stable patients continue treatment indefinitely
- The dose and/or the frequency of IFN Beta administration significantly influences the short-term outcome in patients with RRMS

Multiple Sclerosis Agents

- The route of administration of IFN Beta is not of clinical importance regarding efficacy but does have an impact on the side effect profile
- Based on trial evidence, interferons and glatiramer acetate appear to have similar clinical utility in MS
- The results of the CombiRx trial suggest that glatiramer acetate may be more effective than IFN Beta-1a IM in reducing risk of exacerbations
- comparative data are limited for oral agents
- Cladribine should be reserved for patients who have had an inadequate response to or are unable to tolerate an alternate drug and should not be used for CIS
- Dimethyl fumarate had similar results to glatiramer acetate in a study

Multiple Sclerosis Agents

- Compared to IFN Beta-1a (Avonex), fingolimod (Gilenya) has shown significant efficacy regarding relapse rate and MRI activity
- Fingolimod (Gilenya) also offers the only FDA-approved treatment for pediatric patients with relapsing forms of MS who are ≥10 years of age
- Teriflunomide (Aubagio) appears similar to IFN Beta-1a (Rebif) based on the results of the TENERE trial
- Alemtuzumab (Lemtrada) is approved only for patients who have had an inadequate response to 2 or more drugs indicated for MS
- Alemtuzumab (Tysabri) is available for relapsing forms of MS, but appropriate use is limited due to serious safety concerns
- Ocrevus marks the first medication approved for the treatment of PPMS and is also approved for relapsing MS

Multiple Sclerosis Agents

- The 2018 AAN guidelines (reaffirmed in 2021) state clinicians should offer Ocrevus to PPMS patients who are likely to benefit unless the risks outweigh the benefit
- Kesimpta has been associated with lower annualized relapse rate (ARR) in patients with relapsing MS compared to Aubagio in clinical trials
- In February 2023, ICER published a final evidence report on oral and monoclonal antibody therapies for relapsing forms of MS
- After review of clinical and cost effectiveness through network meta-analysis, it was concluded that both oral therapies and monoclonal antibodies decrease annualized relapse rate (ARR) vs. placebo
- Monoclonal antibodies result in greater reductions in ARR compared to oral medications
- They also had numerically greater effects on confirmed disability progression than oral therapies

Multiple Sclerosis Agents

Clinical and Product Updates

- ICER has published its final evidence report on comparative clinical effectiveness and value of tolebrutinib for treatment of SPMS
- The overall net health benefit for tolebrutinib when compared to best supportive care is rated as promising but inconclusive
- FDA approved cladribine 10 mg tablets by Apotex; it is the first generic for Mavenclad

Opioid Dependence Treatments

ARIZONA HEALTH CARE COST CONTAINMENT SYSTEM

Opioid Dependence Treatments

Class Overview: Buprenorphine Products

- buprenorphine extended-release injection - (Brixadi, Sublocade)
- buprenorphine sublingual tablets

Class Overview: Buprenorphine/Naloxone Combination Products

- buprenorphine/naloxone sublingual film - (Suboxone)
- buprenorphine/naloxone sublingual tablets - (Zubsolv)

Opioid Dependence Treatments

Class Overview: Nalmefene Products

- nalmafene HCl nasal spray - (Opvee)
- nalmefene hydrochloride injection - (Zurnai)

Class Overview: Naloxone Products

- naloxone HCl nasal spray - (Narcan, Narcan OTC, RiVive OTC, Kloxxado, Rextovy)
- naloxone HCl injection - (naloxone syringe, naloxone vial, Zimhi)

Class Overview: Naltrexone Products

- naltrexone HCl tablets
- naltrexone extended-release injectable suspension - (Vivitrol)

Class Overview: Alpha Agonist Product

- lofexidine (Lucemyra)

Opioid Dependence Treatments

- Prescription opioids continue to become increasingly abused
- Approximately 48.4 million people aged 12 years or older in 2024 were considered to have a substance use disorder (SUD)
- This includes 27.9 million people with an alcohol use disorder, 28.2 million people with an illicit drug use disorder, and 4.8 million with an opioid use disorder
- Buprenorphine is a partial agonist at the mu-opioid receptor and an antagonist at the kappa-opioid receptor

Opioid Dependence Treatments

- Naloxone is an antagonist at the mu-opioid receptor
- Buprenorphine/naloxone was co-formulated to prevent patients from abusing buprenorphine in combination with other opioids
- Naltrexone is an opioid antagonist with highest affinity for the mu opioid receptor
- It blocks the effects of opioids by competitive binding at opioid receptors
- Lofexidine is a central alpha-2 agonist that targets the symptoms of opioid withdrawal caused by noradrenergic hyperactivity
- Nalmefene is an antagonist at opioid receptors

Opioid Dependence Treatments

- In clinical trials, few differences in the adverse event profile were noted among Suboxone sublingual film, Zubsolv sublingual tablets, and buprenorphine sublingual tablets
- Comparative data between formulations for induction or maintenance treatment are limited
- There is no maximum duration of maintenance treatment for buprenorphine extended-release injection (Sublocade) or buprenorphine/naloxone sublingual tablet and sublingual and buccal film (Suboxone, Zubsolv)
- For some patients, treatment may continue indefinitely
- Buprenorphine/naloxone sublingual tablet and buccal film should be prescribed based on consideration of visit frequency
- Provision for multiple refills are not recommended early in treatment or without appropriate follow-up

Opioid Dependence Treatments

- Medication-assisted treatment (MAT) for opioid addiction using a buprenorphine-containing product or naltrexone formulation should be accompanied by counseling and psychosocial support
- Narcan, Kloxxado, and Zimhi offer a method for emergency treatment for opioid overdose until medical treatment is obtained
- Alpha2 adrenergic agonists are often used in combination with other agents to target multiple withdrawal symptoms
- In 2016, a meta-analysis was completed to review clinical trials for the effectiveness of alpha2-adrenergic agonists in the management of the acute phase of opioid withdrawal
- There was insufficient data to provide a comparison of the alpha2 adrenergic agonists for effectiveness

Opioid Dependence Treatments

- Per the 2024 DHHS Final Rule, practitioners who are authorized to prescribe schedule III medications, may prescribe buprenorphine for OUD as allowed by state law
- In April 2021, DHHS released new guidelines allowing eligible physicians, physician assistants, nurse practitioners, clinical nurse specialist, certified registered nurse anesthetists, and certified nurse midwives to prescribe buprenorphine to up to 30 patients outside of completing all the previous waiver requirements
- In January 2025, DEA/HHS finalized a rule allowing clinicians to prescribe an initial six-month total supply of schedule III–V MOUD via audio-only telemedicine encounters without a prior in-person exam
- Continuation after 6 months requires audio-video telemedicine under other authorities or an in-person evaluation

Opioid Dependence Treatments

- Per the Society for Adolescent Health and Medicine, all adolescents and young adults with OUD should be offered medication for OUD as a critical component of an integrated treatment approach
- They also recommend treatment without age limitations when treatments are not approved in this younger population
- In general, treatment should include behavioral therapy
- The American Society of Addiction Medicine (ASAM) advises there is no recommended time limit for the pharmacological treatment of OUD
- According to Substance Abuse and Mental Health Services Administration (SAMHSA) and ASAM, no one agent is recommended over another

Opioid Dependence Treatments

Product/Guideline Updates:

- Labeling for opioid-containing products has been updated to include new safety information including risks of:
  - Long-term opioid treatment
  - Toxic leukoencephalopathy
  - Opioid-induced esophageal dysfunction
  - Interactions between opioids and gabapentinoids
  - Seizures (meperidine-containing products)
- Language regarding opioid overdose reversal agents has also been updated

Pancreatic Enzymes

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Pancreatic Enzymes

Class Overview: Products

- Creon
- Pertzye
- Viokace
- Zenpep

Pancreatic Enzymes

- Pertzye, and Zenpep are indicated for the treatment of exocrine pancreatic insufficiency due to cystic fibrosis or other conditions in both adults and children
- Creon is indicated for these conditions, as well as exocrine pancreatic insufficiency due to chronic pancreatitis and pancreatectomy
- Other conditions that may result in exocrine pancreatic insufficiency include ductal obstruction from a neoplasm and gastrointestinal bypass surgery
- Viokace is indicated for the treatment of exocrine pancreatic insufficiency due to chronic pancreatitis or pancreatectomy in combination with a proton pump inhibitor in adults only

Pancreatic Enzymes

Product	Manufacturer	Formulation	Amylase (Units)	Lipase (Units)	Protease (Units)	Notes
Creon® 3,000	AbbVie	Capsule (EC, DR)	15,000	3,000	9,500	For infants, capsule contents may be administered directly to the mouth or with a small amount of applesauce Capsule can be opened for patients unable to swallow
Creon 6,000			30,000	6,000	19,000	
Creon 12,000			60,000	12,000	38,000	
Creon 24,000			120,000	24,000	76,000	
Creon 36,000			180,000	36,000	114,000	

Pancreatic Enzymes

Product	Manufacturer	Formulation	Amylase (Units)	Lipase (Units)	Protease (Units)	Notes
Pertzye™ 4,000	Digestive Care	Capsule (DR)	15,125	4,000	14,375	Only pancreatic enzyme containing bicarbonate-buffered enteric-coated microspheres
Pertzye™ 8,000			30,250	8,000	28,750	Capsule can be opened for patients unable to swallow
Pertzye 16,000			60,500	16,000	57,500	Pertzye 400 (infants up to 12 months): For infants, capsule contents may be administered directly to the mouth or with a small amount of acidic food with a pH ≤ 4.5, such as applesauce.
Pertzye 24,000			90,750	24,000	86,250	Contents should be followed by breast milk or formula but may not be administered directly into breast milk or formula.

Pancreatic Enzymes

Product	Manufacturer	Formulation	Amylase (Units)	Lipase (Units)	Protease (Units)	Notes
Viokace™ 10,440	Allergan/Aptalis	Tablet	39,150	10,440	39,150	Tablets should be swallowed whole and not crushed
Viokace 20,880			78,300	20,880	78,300	Should not be used in pediatric patients; may result in tablet degradation in the gastric environment which may result in suboptimal growth

Pancreatic Enzymes

Product	Manufacturer	Formulation	Amylase (Units)	Lipase (Units)	Protease (Units)	Notes
Zenpep 3,000	Aptalis	Capsule (EC,DR)	14,000	3,000	10,000	For infants, capsule contents may be administered directly to the mouth or with a small amount of acidic food with a PH greater than 4.5 such as applesauce Capsule can be opened for patients unable to swallow
Zenpep 5,000			24,000	5,000	17,000	
Zenpep 10,000			42,000	10,000	32,000	
Zenpep 15,000			63,000	15,000	47,000	
Zenpep 20,000			84,000	20,000	63,000	
Zenpep 25,000			105,000	25,000	79,000	
Zenpep 40,000			168,000	40,000	126,000	

Pancreatic Enzymes

- Pancreatic enzyme supplements differ in enzyme content and bioavailability
- These products have demonstrated favorable risk-benefit profiles in the treatment of exocrine pancreatic insufficiency
- According to consensus guidelines by the CFF, enteric-coated microencapsulated enzymes are the most effective treatment for pancreatic insufficiency in CF
- Dosing of these products should be individualized in accordance with the individual product's prescribing information and the CFF consensus guidelines

Uterine Disorder Treatments

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Uterine Disorder Treatments

Drug (Manufacturer)	Components	FDA Indications
Orilissa (Abbvie)	Elagolix only	• Management of moderate to severe pain associated with endometriosis
Oriahnn (Abbvie)	Elagolix + estradiol + norethindrone (AM) + elagolix (PM)	• Management of heavy menstrual bleeding associated with uterine leiomyomas (fibroids)
Myfembree (Myovant)	Relugolix + estradiol + norethindrone	• Management of heavy menstrual bleeding associated with uterine leiomyomas (fibroids) • Management of moderate to severe pain associated with endometriosis

Uterine Disorder Treatments

- All three agents are oral GnRH receptor antagonists (or combinations with “add-back” hormones)
- They result in decreasing luteinizing hormone (LH)/follicle-stimulating hormone (FSH), which in turn decreases ovarian estrogen/progesterone
- The add-back therapy (estradiol + norethindrone) prevents hypoestrogenic side effects but increases thromboembolic risk
- The duration limit for use of all three agents is 24 months due to bone mineral density (BMD) loss

Uterine Disorder Treatments

- Per the American College of Obstetricians (ACOG), hormonal contraceptives and/or NSAIDs are recommended as first-line for the treatment of endometriosis
- GnRH agents (agonists or antagonists) are considered second-line agents, along with other therapies
- Orilissa and Myfembree offer an oral alternative to injectable GnRH agonists
- They should be used when hormonal therapy fails and when moderate to severe pain persists

Uterine Disorder Treatments

- The International Federation of Gynecology and Obstetrics (FIGO) created best practice guidance in 2025 for medical treatment of fibroids
- Medical therapy is often first line for symptomatic fibroids, especially when fertility preservation or surgery avoidance is desired
- It is used to reduce bleeding symptoms or preoperatively to shrink fibroids and improve anemia before surgery
- GnRH antagonists are considered key modern therapy and is the only class widely approved specifically for fibroids
- They are a first line pharmacologic option and are effective for heavy menstrual bleeding and volume reduction

Uterine Disorder Treatments

- The guideline includes other pharmacological options including the use of:
  - Combined oral contraceptives
  - Oral progestins
  - The levonorgestrel-releasing intrauterine system (LNG-IUS)
- Treatment decisions should be individualized based on symptom severity, location of fibroids, and patient fertility goals

New Drug Reviews

ARIZONA
HEALTH CARE COST
CONTAINMENT SYSTEM

New Drugs

- Lynkuet - elinzanetant
- Redemplo - plozasiran
- Voyxact - sibeprenlimab-szsi
- Cardamyst - etripamil
- Myqorzo - aficamten

Lynkuet (elinzanetant)

- Indicated for the treatment of moderate to severe vasomotor symptoms (VMS) due to menopause
- The recommended dosage is 120 mg orally once daily at bedtime
- Moderate CYP3A4 Inhibitors: Reduce Lynkuet dosage to 60 mg once daily
- Available as 60 mg capsules
- Contraindicated in pregnant patients
- Warnings:
  - CNS depressant effect and daytime impairment
  - Hepatic transaminase elevations
  - Risk of pregnancy loss
  - Risk of seizures

Lynkuet (elinzanetant)

- Avoid concomitant use with:
  - Strong CYP3A4 Inhibitors
  - Grapefruit (juice)
  - Strong and Moderate CYP3A4 Inducers
- Not recommended in patients with:
  - End Stage Renal Disease
  - Moderate to Severe Hepatic Impairment
- Adverse Reactions: headache, fatigue, dizziness and somnolence
- There are no comparative trials

Lynkuet (elinzanetant)

- The efficacy of Lynkuet was based on data from the OASIS 1 and OASIS 2 clinical trials
- They included 796 menopausal women who had at least 50 moderate to severe hot flashes per week
- Participants (mean age, 54.5 years) were randomly assigned to receive Lynkuet 120mg or placebo, once daily at bedtime for 12 weeks
- The primary endpoint was the mean change in frequency and severity of moderate to severe VMS from baseline to weeks 4 and 12, including day and night hot flashes measured using the Hot Flash Daily Diary (HFDD)
- Findings from both trials showed treatment with Lynkuet led to a statistically significant reduction (≥2 hot flashes over 24 hours) in the frequency of moderate to severe VMS compared with placebo

Lynkuet (elinzanetant)

- Change from baseline to week 4:
  - OASIS 1: -7.60 vs -4.31 (least squares [LS] mean difference vs placebo, -3.29 [95% CI, -4.47, -2.10]; *P* <.0001)
  - OASIS 2: -8.58 vs -5.54 (LS mean difference vs placebo, -3.04 [95% CI, -4.40, -1.68]; *P* <.0001)
- Change from baseline to week 12:
  - OASIS 1: -8.66 vs -5.44 (LS mean difference vs placebo, -3.22 [95% CI, -4.81, -1.63]; *P* <.0001).
  - OASIS 2: -9.72 vs -6.48 (LS mean difference vs placebo, -3.24 [95% CI, -4.60, -1.88]; *P* <.0001)

Lynkuet (elinzanetant)

- In addition, a statistically significant reduction in severity of moderate to severe VMS was observed with Lynkuet vs placebo in both trials
- Change from baseline to week 4:
  - OASIS 1: -0.73 vs -0.40 (least squares [LS] mean difference vs placebo, -0.33 [95% CI, -0.44, -0.23]; *P* <.0001)
  - OASIS 2: -0.75 vs -0.53 (LS mean difference vs placebo, -0.22 [95% CI, -0.34, -0.09]; *P* =.0003)
- Change from baseline to week 12:
  - OASIS 1: -0.92 vs -0.52 (LS mean difference vs placebo, -0.40 [95% CI, -0.54, -0.25]; *P* <.0001)
  - OASIS 2: -0.91 vs -0.62 (LS mean difference vs placebo, -0.29 [95% CI, -0.44, -0.14]; *P* <.0001)

Redemplo (plozasiran)

- Indicated as an adjunct to diet to reduce triglycerides (TG) in adults with familial chylomicronemia syndrome (FCS)
- The recommended dosage is 25 mg injected subcutaneously once every 3 months
- Available as 25 mg/0.5 mL injection solution in a single-dose pre-filled syringe
- Adverse Reactions: hyperglycemia, headache, nausea, and injection site reaction
- There are no comparative trials

Redemplo (plozasiran)

- The efficacy of Redemplo was based on data from the randomized, placebo-controlled, double-blind, phase 3 PALISADES trial
- The study enrolled adults with genetically confirmed or clinically diagnosed FCS on a low-fat diet, defined as ≤20 grams of fat per day
- Participants were randomly assigned to receive 4 doses of Redemplo 25mg (n=26) or matching placebo (n=25) subcutaneously once every 3 months for 12 months
- The primary endpoint was the percent change from baseline in fasting TG at month 10

Redemplo (plozasiran)

- Findings showed a significant reduction in median TG levels with Redemplo vs placebo (pooled) at month 10 (-80% vs -17%; difference, -59% [95% CI, -90, -28]; *P* <.0001)
- A consistent TG lowering effect was observed with Redemplo over the 12-month treatment period
- The numerical incidence of acute pancreatitis was lower in patients who received Redemplo vs those who received placebo (8% vs 20%)

Voyxact (sibeprenlimab-szsi)

- Indicated to reduce proteinuria in adults with primary immunoglobulin A nephropathy (IgAN) at risk for disease progression
- This indication is approved under accelerated approval based on reduction of proteinuria
- Recommended dosage: 400 mg injected subcutaneously once every 4 weeks
- Available as 400 mg/2 mL (200 mg/mL) injection in a single-dose prefilled syringe
- Contraindication: serious hypersensitivity to sibeprenlimab-szsi or any excipients in Voyxact

Voyxact (sibeprenlimab-szsi)

- Warnings:
  - Immunosuppression - Increased risk of infections and immunization risks
- Adverse Reactions: upper respiratory tract infection and injection site erythema
- There are no comparative trials
- VISIONARY was a phase 3, global, randomized, double-blind, placebo-controlled trial
- The study enrolled adults with biopsy-confirmed IgAN, eGFR ≥30 mL/min/1.73 m^2, and persistent proteinuria despite optimized supportive care
- Patients were randomized 1:1 to receive Voyxact (n=259) or placebo (n=251) subcutaneously every 4 weeks

Voyxact (sibeprenlimab-szsi)

- Participants also remained on a stable and maximally tolerated dose of ACE inhibitors and/or ARBs with or without an SGLT2 inhibitor throughout the study
- Primary analysis was conducted in the first 320 patients reaching the 9-month visit (Voyxact, n=152; placebo, n=168)
- Key efficacy results were 50% reduction in 24-hour urine protein-to-creatinine ratio (uPCR) in the Voyxact group vs 2% increase for placebo at 9 months (96.5% CI, 43%, 58%; *P*<0.0001)
- Additional clinical findings include faster hematuria resolution (82.5% negative at Week 48 with Voyxact vs 52.6% with placebo)

Cardamyst (etripamil)

- Indicated for the conversion of acute symptomatic episodes of paroxysmal supraventricular tachycardia (PSVT) to sinus rhythm in adults
- Initial dosage is 70 mg administered as two nasal sprays, one spray into each nostril
- Repeated dosage (if needed): should symptoms persist for 10 minutes after administration of Cardamyst, a second dose of 70 mg should be administered as two nasal sprays, one spray into each nostril
- Available as a nasal spray, 70 mg per device

Cardamyst (etripamil)

- Contraindications:
  - Hypersensitivity to Cardamyst or any of its components
  - Heart failure - New York Heart Association (NYHA) Class II to IV
  - Wolff-Parkinson-White (WPW), Lown-Ganong-Levine (LGL) syndromes, or manifest pre-excitation (delta wave) on a 12-lead ECG
  - Sick sinus syndrome (except in patients with a permanent pacemaker)
  - Second degree atrioventricular (AV) Mobitz 2 block or higher degree of AV block

Cardamyst (etripamil)

- Warning: Syncope
- Adverse Reactions: nasal discomfort, nasal congestion, rhinorrhea, throat irritation, and epistaxis
- There are no comparative trials
- RAPID was a randomized, double-blind, placebo-controlled phase 3 trial
- The study evaluated the safety and efficacy of Cardamyst in patients with a history of symptomatic PSVT
- Participants (N=692) were randomly assigned 1:1 to receive a self-administered dose of intranasal Cardamyst 70mg or placebo in a medically unsupervised setting during an episode of perceived PSVT
- A second dose was self-administered if symptoms persisted 10 minutes after the first dose

Cardamyst (etripamil)

- The primary endpoint was time-to-conversion of confirmed PSVT to sinus rhythm for at least 30 seconds within 30 minutes of the first dose
- In patients with a confirmed episode of PSVT (n=184), 64% of those in the Cardamyst arm converted to sinus rhythm within 30 minutes compared with 31% of those who received placebo (HR, 2.6 [95% CI, 1.7-4.2]; *P* <.001)
- The median time-to-conversion was 17.2 minutes (95% CI: 13.4, 26.5) with Cardamyst vs 53.5 minutes (95% CI: 38.7, 87.3) with placebo
- At 300 minutes, the conversion remained favorable toward Cardamyst (HR, 1.7 [95% CI, 1.2-2.4])
- Among the patients who self-administered Cardamyst for a perceived episode of PVST (n=255), 71 did not have a confirmed PSVT
- In an analysis assuming that all 71 PSVT unconfirmed patients did not convert, conversion to sinus rhythm still remained significantly higher with Cardamyst vs placebo (50% vs 23%; HR, 2.6 [95% CI, 1.6-4.1])

Myqorzo (aficamten)

- Indicated for the treatment of adults with symptomatic obstructive hypertrophic cardiomyopathy (oHCM) to improve functional capacity and symptoms
- Starting dose is 5 mg orally once daily
- The maintenance dose is individualized based on the patient's left ventricular ejection fraction (LVEF) and left ventricular outflow tract gradient (LVOT-G)
- The maximum dose is 20 mg once daily
- Available as 5 mg, 10 mg, 15 mg, and 20 mg film-coated tablets
- Contraindication: Concomitant rifampin use

Myqorzo (aficamten)

- Boxed Warning: Risk of heart failure (available only through the Myqorzo REMS Program)
- Warning: Drug interactions leading to increased risk of heart failure or loss of effectiveness
- Adverse Reaction: hypertension
- There are no comparative trials
- SEQUOIA-HCM was a randomized, double-blind, placebo-controlled phase 3 trial
- It included adults with symptomatic class II and III oHCM
- Additional Inclusion Criteria:
  - LVEF ≥60%
  - Resting peak LVOT-G ≥30mmHg and a post-Valsalva peak
  - LVOT-G ≥50 mmHg at screening

Myqorzo (aficamten)

- Participants were randomly assigned 1:1 to receive Myqorzo (n=142) or placebo (n=140) once daily for 24 weeks
- The primary endpoint was the change from baseline to week 24 in mean peak oxygen uptake (pVO_2) measured by cardiopulmonary exercise testing
- Findings showed Myqorzo led to a statistically significant improvement in exercise capacity compared with placebo (change from baseline in pVO_2: 1.7mL/min/kg vs 0.0mL/min/kg; least squares mean difference, 1.7 [95% CI, 1.0-2.4]; *P* <.0001)
- Results also showed Myqorzo was associated with statistically significant improvements in the following secondary endpoints vs placebo at week 24 (all *P* <.0001):

Myqorzo (aficamten)

- Mean change from baseline in Kansas City Cardiomyopathy Questionnaire Clinical Summary Score: 11.6 vs 4.3 (difference, 7.3 [95% CI, 4.6-10.1])
- Mean change from baseline in Valsalva LVOT-G: -46.7mmHg vs 2.2mmHg (difference, -48.8 [95% CI, -55.7, -42.0])
- Mean duration of septal reduction therapy eligibility: 35 days vs 113 days (difference, -78 [95% CI, -100, -56])
- Mean change from baseline in total workload during cardiopulmonary exercise testing: 13.1 Watts vs 0.9 Watts (difference, 12.2 [95% CI, 6.3-18.1])
- Proportion of patients with at least 1 class improvement: 58.5% vs 24.3% (odds ratio, 4.4 [95% CI, 2.6-7.6])
- Proportion of patients with Valsalva LVOT-G less than 30mmHg: 49.3% vs 3.6% (odds ratio, 22.9 [95% CI, 8.8-59.6])

Break and Executive Session

ARIZONA
HEALTH CARE COST
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Public Therapeutic Class Votes

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Future Meeting Date: October 7, 2026

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