ARIZONA
HEALTH CARE COST
CONTAINMENT SYSTEM

AHCCCS Pharmacy and Therapeutics Committee

May 21, 2025

AHCCCS P&T Agenda

- Welcome and Introductions
- Minutes Review & Vote
- Legislative Report Update
- Supplemental Rebate Class Reviews
- New Drug Reviews
- Executive Session
- Public Therapeutic Class Votes
- Biosimilar Update
- Meeting Adjournment

Welcome and Introductions

- Suzi Berman, RPh, Pharmacy Director, AHCCCS
  - Minutes Review and Vote - P&T January 15, 2025
  - Review
  - Vote

HB2903 Report Update

ARIZONA HEALTH CARE COST CONTAINMENT SYSTEM

HB2903 Report Request

- HB2903 required AHCCCS to submit report to the Governor's Office, , the President of the Senate, the Speaker of the House of Representatives, the chairperson of the Health and Human Services Committee, or its successor, in the senate and the chairperson of the Health Committee, or its successor, in the House of Representatives, director of the Joint Legislative Budget Committee and the director of the Governor's Office of Strategic Planning and Budgeting and shall provide a copy of this report to the Secretary of State
- Federal Fiscal Years 2020–2024 – Referred to as Contract Year (CY)
- Drug Classes Included in the Report Request:
    - Antidepressants
    - Antipsychotics
    - Anxiolytics
    - Stimulants
    - Sedative Hypnotics

HB2903 Report Requests For All Therapeutic Classes

- Annual aggregate gross amount spent for each MH medication class;
- Annual aggregate net amount spent by this state for each MH medication class after rebates without disclosing any information about manufacturer-negotiated supplemental rebate agreements for any specific drug;
- Average annual cost by class for generic and non-generic MH medications;

HB2903 Annual Aggregate Expenditures For Therapeutic Classes

CY	Antianxiety Agents	Antidepressants	Antipsychotics	Sedative Hypnotics	Stimulants
2020	$ 3,716,133	$ 17,285,019	$ 174,867,774	$ 1,785,264	$ 58,454,590
2021	$ 4,029,331	$ 19,564,026	$ 194,931,464	$ 1,964,525	$ 64,483,986
2022	$ 4,706,100	$ 23,399,257	$ 210,687,453	$ 2,279,172	$ 73,700,723
2023	$ 4,079,124	$ 23,686,655	$ 213,001,401	$ 2,001,629	$ 81,221,516

HB2903 Annual Aggregate Expenditures For Therapeutic Classes Net of the Federal Rebate

CY	Antianxiety Agents	Antidepressants	Antipsychotics	Sedative Hypnotics	Stimulants
2020	$3,511,498	$14,424,165	$69,215,669	$843,714	$13,956,761
2021	$3,843,923	$16,586,604	$67,452,918	$754,489	$12,114,974
2022	$4,539,346	$20,140,357	$63,909,554	$803,588	$11,827,629
2023	$3,917,268	$20,659,011	$52,880,557	$835,966	$10,849,768

Average Annual Cost by Therapeutic Class for Generic and Non-Generic Utilization

	CY	2020	2021	2022	2023
Antianxiety Agents	Brand	$ 31,949	$ 60,755	$ 76,613	$ 80,273
	Generic	$ 3,684,184	$ 3,968,576	$ 4,629,487	$ 3,998,852
Antidepressants	Brand	$ 2,765,879	$ 3,548,378	$ 6,167,914	$ 9,304,204
	Generic	$ 14,519,140	$ 16,015,648	$ 17,231,343	$ 14,382,451
Antipsychotics	Brand	$ 159,911,618	$ 179,817,972	$ 194,564,979	$ 197,576,080
	Generic	$ 14,956,156	$ 15,113,491	$ 16,122,473	$ 15,425,320
Sedative Hypnotics	Brand	$ 1,084,765	$ 1,247,324	$ 1,544,800	$ 1,060,054
	Generic	$ 700,499	$ 717,200	$ 734,372	$ 941,575
Stimulants	Brand	$ 48,321,097	$ 53,069,168	$ 61,084,783	$ 70,537,852
	Generic	$ 10,133,493	$ 11,414,818	$ 12,615,940	$ 10,683,664

HB2903 Report Requests For Antidepressants And Antipsychotic Therapeutic Classes

- For antipsychotic and antidepressant medications:
  - Total number of prior authorizations (PAs) submitted for nonpreferred antipsychotic and nonpreferred antidepressant medications,
  - Percentage of PA approvals and denials,
  - Generic antipsychotic and generic antidepressant medication utilization percentages, and
- Total amount of antipsychotic and antidepressant medication claims.

Number of Prior Authorizations Submitted & Prescription Claim Count For Antidepressants and Antipsychotics

Prior Authorizations By CY	2020	2021	2022	2023
Antidepressants - Non-Preferred	5,726	4,864	6,372	8,652
Antipsychotics - Non-Preferred	7,037	5,933	6,987	9,644

RX Claim By CY	2020	2021	2022	2023
Antidepressants	1,234,326	1,420,000	1,546,787	1,558,247
Antipsychotics	645,602	689,305	731,537	758,936

Generic Antidepressants and Antipsychotics Utilization Percentages

CY	2020	2021	2022	2023
Antidepressants	99.5%	99.5%	99.4%	99.3%
Antipsychotics	85.2%	85.3%	85.7%	87.4%

For CY 2023:

- Antidepressants
  - Brand drug costs equals $9.3M representing 39.3% of the cost and less than 1% of the utilization.
  - Generic drug costs equals $14.4M representing 60.7% of the cost and 99.3% of utilization as noted above.
- Antipsychotics
  - Brand drug costs equals $197M representing 92.8% of the cost and less than 12.6% of the utilization.
  - Generic drug costs equals $15M representing 7.2% of the cost and 87.4% of utilization as noted above.

Prior Authorizations Approved and Denied For Non-Preferred Medications

Contract Year	2020		2021		2022		2023	
	% Approved	% Denied	% Approved	% Denied	% Approved	% Denied	% Approved	% Denied
Anti-depressants	34.4%	31.6%	37.8%	38.9%	37.7%	34.9%	36.9%	29.3%
Anti-psychotics	40.1%	29.1%	42.0%	35.7%	37.5%	36.7%	41.9%	32.1%

Denial Prior Authorization Reasons

- Member has alternate insurance coverage.
- Member insurance coverage terminated.
- Documentation does meet medical necessity criteria.
- The request is for an experimental use of the drug.
- The prescriber is out of network.
- The pharmacy is out of network.
- Documentation submitted is incomplete, additional information was requested, and a response was not received.
- Request is for a diagnosis that is off label use and compendia does not support the use.
- Therapeutic duplication.
- Dosage exceeds the FDA Allowable Maximum and compendia does not support the increased dose.

Resolved Prior Authorization Reasons

- Member is enrolled in a different MCO or FFS.
- Member AHCCCS enrollment terminated.
- Prior authorization submitted is a duplicate of one already received.
- Prescriber is contacted and PA is resolved through an educational process.
- Prescriber unaware of preferred agents.
- Prescriber withdraws the submitted PA from the PA process.
- Drug covered- generic required- physician notified and changed to the generic.
- PA is not required for the requested drug.
- Request withdrawn by the prescriber.
- Member is not enrolled in the AHCCCS program

Contract Year 2023 PA Stats For Antidepressants

- 8652 PAs Received For Antidepressants
  - Approved – 3192
  - Denied – 2535
    - The number PAs denied for not meeting medical necessity criteria was 1367 and 1136 were denied for other reasons.
      - The medical necessity denial rate was 15.8%
    - Resolved – 2925
  - 1,558,247 Antidepressant Prescriptions were filled in 2023
    - Submitted prior authorization requests represent a small subset of drugs, members and antidepressant prescription utilization.
    - Over 99% of antidepressant prescription utilization did not require prior authorization.

Contract Year 2023 PA Stats For Antipsychotics

- 9644 PAs Received For Antipsychotics
  - Approved – 4041
  - Denied – 3096
    - The number PAs denied for not meeting medical necessity criteria was 2204 and 892 were denied for other reasons.
      - The medical necessity denial rate was 22.8%
  - Resolved – 2507
  - 758,936 Antipsychotics Prescriptions were filled in 2023
    - Submitted prior authorizations requests represent a small subset of drugs, members and antipsychotic prescription utilization.
    - Over 99% of antipsychotic prescription utilization did not require prior authorization.

Pharmacy Dept Email Address - AHCCCSPharmacyDept@azahcccs.gov

Prime Therapeutics Drug Class Reviews

Umang Patel, PharmD, APh

ARIZONA HEALTH CARE COST CONTAINMENT SYSTEM

Prime Therapeutics Class Reviews

Classes for Review: Supplemental Rebate Classes

- Analgesics, Long-Acting Narcotic
- Antibiotics, Inhaled
- Antimigraine Agents, Other
- Antipsychotics, Atypical Long-Acting Injectable
- Antipsychotics, Oral Atypical (2nd Gen Only)
- Colony Stimulating Factors
- COPD Agents
- Cytokine and CAM Antagonists
- Glucagon Agents
- Glucocorticoids, Inhaled
- Growth Hormone
- Hepatitis C Agents
- HIV AIDS
- Hypoglycemics (Insulin and Related Agents)
- Hypoglycemics, Incretin Mimetics/Enhancers
- Immunologics (Immunomodulators, Atopic Dermatitis and Immunomodulators, Asthma)
- Movement Disorders
- Multiple Sclerosis Agents
- Opioid Dependence Treatments
- Pancreatic Enzymes
- Stimulants and Related Agents

Analgesics, Long-Acting Narcotic

ARIZONA HEALTH CARE COST CONTAINMENT SYSTEM

Analgesics, Narcotics Long Acting

Class Overview: Products

- buprenorphine (buprenorphine transdermal, Butrans)
- buprenorphine HCl (Belbuca)
- fentanyl transdermal
- hydrocodone bitartrate (Hysingla ER & Zohydro ER)
- hydromorphone HCl (Exalgo, hydromorphone ER)
- methadone HCl (methadone concentrate, solution, tablet & sol tab)

Analgesics, Narcotics Long Acting

Class Overview: Products

- morphine sulfate (Arymo ER, Morphabond ER, morphine ER capsule, morphine ER tablet, MS Contin)
- oxycodone HCl (oxycodone ER, Oxycontin)
- oxycodone myristate (Xtampza ER)
- oxymorphone HCl (oxymorphone ER)
- tapentadol HCl (Nucynta ER)
- tramadol HCl (Conzip, tramadol ER (gen. Conzip, Ryzolt & Ultram))

Analgesics, Narcotics Long Acting

- The following agents have demonstrated abuse-deterrence in studies, thus meeting FDA requirements for abuse-deterrent formulations:
  - Hysingla ER tablets
  - Oxycontin biconcave tablets
  - Oxycodone ER (authorized generics of Oxycontin) tablets
  - Xtampza ER capsules
- Although hydromorphone ER, tapentadol ER (Nucynta ER), and hydrocodone ER (Zohydro ER) have abuse-deterrent properties, they have not been approved by the FDA as abuse-deterrent formulations

Analgesics, Narcotics Long Acting

- Data from 2019 demonstrated that approximately 20.4% of adults report chronic pain in the US.
- Historically, data have suggested that pain may be undertreated, but newer estimates imply that opioid treatment for pain may be overutilized.
- Opioid agonists reduce pain through interaction with opioid mu-receptors located in the brain, spinal cord, and smooth muscle.
- The primary site of therapeutic action is the central nervous system (CNS).
- Opioid agonists produce respiratory depression by direct action on the brain stem respiratory center.
- Buprenorphine is a partial agonist/antagonist of opioid receptors.

Analgesics, Narcotics Long Acting

- Naltrexone is a centrally-acting mu-receptor antagonist that reverses the analgesic effects of mu-receptor agonists by competing for binding sites with opioids.
- No clinical data exist that distinguish analgesic efficacy of any of these products from the others.
- Pain management must be individualized and patients who do not respond to one opioid may respond to another.
- Abuse deterrent formulations do not enhance analgesic properties.
- All opioids can be abused and are subject to illicit use.
- Abuse deterrent formulations are intended to make misuse more difficult, but do not affect diversion.

Analgesics, Narcotics Long Acting

- In 2022, the American Society of Clinical Oncology (ASCO) published guidelines for the use of opioids for adults with pain from cancer or cancer treatment.
- Opioids are recommended to be offered to patients with moderate to severe pain related to cancer or active treatment unless a contraindication is present.
- No specific agent is recommended over another.
- Use of these agents should be initiated as needed at the lowest possible dose to achieve analgesia with early evaluation and frequent titration.
- Adverse events to these agents should be monitored, prevented, and managed as appropriate.
- Patients with substance use disorders should receive collaborative care with specialists in order to establish the optimal management plan.

Analgesics, Narcotics Long Acting

- In 2022, the Centers for Disease Control and Prevention (CDC) released guidelines for prescribing opioids for pain outside of sickle cell disease, cancer, palliative, and end-of-life care.
- There are 5 guiding principles intended to inform implementation of the updated guideline recommendations; these are:
  - (1) Acute, subacute, and chronic pain needs to be assessed appropriately and treated regardless of whether opioids are a component of the treatment plan
  - (2) Recommendations are voluntary and designed to support individualized, patient centered care
  - (3) A multimodal and multidisciplinary approach should be used for pain management
  - 4) The guidelines should not be applied beyond intended use resulting in adverse consequences for patients
  - 5) Healthcare professionals and health systems should be aware of health inequities and provide appropriate communication and support for all persons
- The updated guidelines also address acute pain and subacute pain, as well as focus on health disparities that are present in the treatment of pain.

Antibiotics, Inhaled

ARIZONA HEALTH CARE COST CONTAINMENT SYSTEM

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.
- The typical manifestation of CF involves progressive obstructive lung disease that has been 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 in CF therapy to control the progression of the disease.

Antibiotics, Inhaled

- The Cystic Fibrosis Foundation (CFF) recommends inhaled antibiotic therapy for the treatment of initial or new growth of P. aeruginosa, with preference for tobramycin for 28 days.
- Chronic use of 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

- The CF Foundation also recommends alternate-month administration of both tobramycin and aztreonam in patients persistently infected with P. aeruginosa.
- In 2016, a clinical guideline for CF in preschool-aged children was developed by the CFF.
- For this patient population, CFF recommends oral, inhaled, and/or IV antibiotics for treatment of pulmonary exacerbations and every other month administration of 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.

Antimigraine Agents, CGRP

ARIZONA HEALTH CARE COST CONTAINMENT SYSTEM

Antimigraine Agents, CGRP

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
galcanezumab-gnlm (Emgality)	Eli Lilly	Preventive treatment of migraine in adults Treatment of episodic cluster headache in adults
rimegepant (Nurtec® ODT)	Biohaven	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, CGRP

- Migraines account for 10% to 20% of all headaches in adults and affect over 39 million men, women, and children in the United States
- 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
- Studies suggest that 38% to 50% of migraineurs are candidates for preventive therapy

Antimigraine Agents, CGRP

- Cluster headache (CH) is a severe, primary headache disorder characterized by extreme pain on one side of the head and autonomic symptoms (e.g., nasal congestion, lacrimation)
- CH periods can persist for weeks to months with daily or more frequent attacks of 15 to 180 minutes in duration
- 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, CGRP

- The American Academy of Neurology (AAN) and the American Headache Society (AHS) advise that antiepileptic drugs (divalproex sodium, sodium valproate, topiramate) and beta-blockers (metoprolol, propranolol, timolol) are established as *effective* in migraine prevention
- Antidepressants (amitriptyline, venlafaxine) and beta-blockers (atenolol, nadolol) are *probably effective* in migraine prevention
- In 2018, the FDA approved three calcitonin gene-related peptide (CGRP) inhibitors: erenumab-aooe (Aimovig), fremanezumab-vfrm (Ajovy), and galcanezumab-gnlm (Emgality), for preventative treatment of migraines in adults
- Since December 2019, the FDA has approved 4 additional CGRP inhibitors: eptinezumab-jjmr (Vyepti), rimegepant (Nurtec ODT), ubrogepant (Ubrelvy), and atogepant (Qulipta), as well as the 5-HT 1F receptor agonist lasmiditan (Reyvow)

Antimigraine Agents, CGRP

The AHS recommends initiating CGRP inhibitors for migraine prophylaxis in patients ≥ 18 years of age with the following:

1. Diagnosis of migraine (with or without aura) experiencing 4 to 7 monthly headache days with moderate disability and inability to tolerate or inadequate response to a 6-week trial of at least 2 oral prophylactic agents
2. Diagnosis of migraine (with or without aura) experiencing 8 to 14 monthly headache days and inability to tolerate or inadequate response to a 6-week trial of at least 2 oral prophylactic agents
3. Diagnosis of chronic migraine and either inability to tolerate or inadequate response to a 6-week trial of at least 2 oral prophylactic agents or at least 6 months of onabotulinumtoxinA treatment

Antimigraine Agents, CGRP

The AHS recommends the following for the treatment of Cluster Headaches:

1. Subcutaneous sumatriptan (SC), zolmitriptan nasal spray, and 100% oxygen for the acute treatment of episodic or chronic CH
2. Therapies considered probably effective for episodic and chronic CH include sumatriptan nasal spray and oral zolmitriptan
3. Galcanezumab-gnlm (Emgality) is the first FDA-approved treatment for episodic CH that decreases the frequency of acute attacks and was not available at the time of the AHS guideline development

Antimigraine Agents, CGRP

Product/Guideline Updates:

- FDA has approved Symbravo, a combination of the NSAID, meloxicam and the triptan, rizatriptan, for the acute treatment of migraine with or without aura in adults.
- Symbravo should only be used where a clear diagnosis of migraine has been determined; it is not indicated for the preventive treatment of migraine or for the treatment of cluster headache.
- Product will be supplied as oral tablets in the strengths of 20 mg meloxicam/10 mg rizatriptan.
- The recommended dose is 1 tablet by mouth as needed (max daily dose=1 tablet).
- Boxed warning for risk of serious CV and GI events.

Antimigraine Agents, CGRP

Product/Guideline Updates:

- American College of Physicians (ACP) has published a clinical practice guideline on use of pharmacological treatment for **prevention** of episodic migraine in nonpregnant adults in outpatient settings.
- Guideline suggests monotherapy with a beta-adrenergic blocker (e.g., metoprolol, propranolol), valproate, venlafaxine, or amitriptyline.
- Patients who do not tolerate or have an inadequate response to these meds are suggested to be given monotherapy with a calcitonin gene-related peptide (CGRP) antagonist-gepant or CGRP monoclonal antibody.
- Patients who do not respond to any of these therapies are suggested to be prescribed topiramate.

Antimigraine Agents, CGRP

Product/Guideline Updates:

- American College of Physicians (ACP) has published a guideline on pharmacologic **treatments** for acute episodic migraine headache in the outpatient setting.
- A triptan is recommended to be added to an NSAID to treat moderate to severe acute episodic migraine headache for nonpregnant adults who do not have a sufficient response to an NSAID (strong recommendation; moderate-certainty evidence).
- It is suggested to add a triptan to APAP for the treatment of moderate to severe acute episodic migraine headache for nonpregnant adults who do not have a sufficient response to APAP (conditional recommendation; low-certainty evidence).

Antipsychotics

ARIZONA HEALTH CARE COST CONTAINMENT SYSTEM

Antipsychotics

Class Overview - Product indications include:

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

Antipsychotics

Class Summary:

- Inconclusive evidence remains regarding the overall effectiveness of second-generation antipsychotics compared to first generation agents in terms of primary outcomes as seen in changes in rating scale scores, particularly when considering the length of many clinical studies
- However, second generation antipsychotics are associated with less extrapyramidal symptoms (EPS) than first generation antipsychotics
- The question of long-term adverse events with second generation antipsychotic use remains unresolved, particularly related to metabolic disorders
- Second generation antipsychotics have largely replaced first generation antipsychotics in the treatment of psychotic disorders, but the long-term effectiveness and adverse event profiles of these products have not been shown to be definitively better

Antipsychotics

Class Summary:

- 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 reports of severe neutropenia and seizures occurring, patients taking it must have regular white blood cell and absolute neutrophil counts closely monitored
- 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 Long-Acting Injectable

ARIZONA HEALTH CARE COST CONTAINMENT SYSTEM

Antipsychotics, Atypical Long-Acting 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®)	Janssen	Schizoaffective disorder (monotherapy and as an adjunct to mood stabilizers or antidepressants)	X	--

Antipsychotics, Atypical Long-Acting 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®)	Janssen	--	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	--

Antipsychotics, Atypical Long-Acting Injectable

Drug	Manufacturer	Other Indications	Schizophrenia	Bipolar Disorder
Second Generation Antipsychotics – Long Acting Injectable				
paliperidone palmitate (Invega Hafyera™)	Janssen	--	X Treatment of schizophrenia in adults after they have been adequately treated with: • A once-a-month paliperidone palmitate extended-release (PP1M) injectable suspension (e.g., Invega Sustenna®) for ≥ 4 months OR • An every-3-month paliperidone palmitate extended-release (PP3M) injectable suspension (e.g., Invega Trinza®) for ≥ one 3 month cycle	--

Antipsychotics, Atypical Long-Acting Injectable

Class Summary:

- 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, with the exception of injection-site pain, which was lower with every 2-week formulations compared to every 4-week formulations
- Overall, data is very limited

Antipsychotics, Atypical Long-Acting Injectable

Product/Guideline Updates:

- FDA has approved the atypical antipsychotic paliperidone palmitate as Erzofri ER injectable suspension for treatment of schizophrenia in adults and schizoaffective disorder in adults as monotherapy & as an adjunct to mood stabilizers or antidepressants.
- Product will be available as a 39 mg/0.25 mL, 78 mg/0.5 mL, 117 mg/0.75 mL, 156 mg/mL, 234 mg/1.5 mL, & 351 mg/2.25 mL ER injectable suspension.
- Erzofri is administered as a monthly IM injection by a Healthcare Practitioner starting with 351 mg on day 1, then 39 mg to 234 mg monthly for schizophrenia, or 78 mg to 234 mg monthly for schizoaffective disorder.

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 (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)
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)

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)	asenapine (Saphris®)
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 (Fazaclo®)	Generic, Jazz						
clozapine (Versacloz®)	Jazz / 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	--	--	--	--
lurasidone (Latuda®)	generic, Sunovion	--	X (ages ≥ 13 years)	--	X (ages ≥ 10 years as monotherapy and in combination with lithium or valproate)	--	--
olanzapine (Zyprexa®)	Generic, Eli Lilly	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 (Symbyax®)	Generic, Eli Lilly	Treatment-resistant depression	--	--	X (ages ≥ 10 years for acute episodes)	--	--
olanzapine/ samidorphan (Lybalvi™)	Alkermes		X		X		
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 ≥ 13years)	X (ages ≥ 10 years as monotherapy; adults in combination with lithium or valproate)	--	X (ages ≥ 10 years as monotherapy; adults in combination with lithium or valproate)	--
ziprasidone (Geodon®)	generic., Pfizer	--	X	X (acute episodes)	--	X (acute episodes)	X (in combination with lithium or divalproex)

Antipsychotics, Second Generation Oral

Product/Guideline Updates:

- FDA approved Cobenfy (xanomeline/trospium chloride), a combination of xanomeline, a muscarinic agonist, and trospium chloride, a muscarinic antagonist, for the treatment of schizophrenia in adults.
- Approved as oral capsules (xanomeline/trospium chloride) in 50mg/20mg, 100mg/20mg, and 125mg/30mg strengths.
- Recommended starting dosage is 50mg/20mg orally twice daily for ≥ 2 days, then increase the dosage to 100mg/20mg twice daily for ≥ 5 days; may increase to 125 mg/30 mg orally twice daily based on patient tolerability and response.
- Most common adverse effects were nausea, dyspepsia, constipation, vomiting, hypertension, abdominal pain, diarrhea, tachycardia, dizziness, and gastrointestinal reflux disease.

Colony Stimulating Factors

ARIZONA HEALTH CARE COST CONTAINMENT SYSTEM

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)*
eflapegrastim-xnst (Rolvedon®)[1]	Spectrum	X	--	--	--	--	--
filgrastim (Neupogen®)[2]	Amgen	X	X	X[a]	X	X	X
filgrastim-aafi (Nivestym®)[*3]	Pfizer	X	X	X[a]	X	X	--
filgrastim-ayow (Releuko®)[*4]	Amneal	X	X	X[a]	--	X	--
filgrastim-sndz (Zarxio®)[*5]	Sandoz	X	X	X[a]	X	X	--
pegfilgrastim (Neulasta®)[6]	Amgen	X	--	--	--	--	X
pegfilgrastim-apgf (Nyvepria®)[†7]	Pfizer	X	--	--	--	--	--
pegfilgrastim-cbqv (Udenyca®)[†8]	Coherus	X	--	--	--	--	X
pegfilgrastim-jmdb (Fulphila®)[†9]	Mylan/Biocon	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-bmez (Ziextenzo®)†[10]	Sandoz	X	--	--	--	--	--
pegfilgrastim-fpgk (Stimufend®)†[11]	Fresenius Kabi	X	--	--	--	--	X
pegfilgrastim-pbbk (Fylnetra®)†[12]	Amneal	X	--	--	--	--	--
sargramostim (Leukine®)[13]	Partner	--	X	X[b]	X	--	X
tbo-filgrastim (Granix®)[14]	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
- Eflapegrastim-xnst (Rolvedon), filgrastim (Neupogen), filgrastim-aafi (Nivestym), filgrastim-ayow (Releuko), filgrastim-sndz (Zarxio), pegfilgrastim (Neulasta), pegfilgrastim-apgf (Nyvepria), pegfilgrastim-cbqv (Udenyca), pegfilgrastim-jmdb (Fulphila), pegfilgrastim-bmez (Ziextenzo), pegfilgrastim-fpgk (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 to the originator products, filgrastim and pegfilgrastim are now available

Colony Stimulating Factors

- The NCCN 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
- Due to their recent approvals, pegfilgrastim-apgf (Nyvepria), filgrastim-ayow (Releuko), pegfilgrastim-fpgk (Stimufend), and pegfilgrastim-pbbk (Fylnetra) were not addressed by NCCN in their v1.2023 guidance
- Eflapegrastim-xnst is included in the guideline and can be administered 24 hours after cytotoxic chemotherapy, but not within 14 days prior to 24 hours after chemotherapy

Colony Stimulating Factors

- NCCN guidelines recommend that high-risk patients receive prophylactic CSF regardless of the intent of treatment
- 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

Colony Stimulating Factors

Product Update:

- FDA approved a new indication for Fylnetra (pegfilgrastim-pbbk) to increase survival in patients acutely exposed to myelosuppressive doses of radiation (Hematopoietic Subsyndrome of Acute Radiation Syndrome).
- Recommended dosage for adults and ped pts weighing ≥ 45 kg is two doses, 6 mg each, administered SC one week apart.
- For pediatric patients weighing < 45 kg, the recommended dose is weight-based:
  - 0.1 mg/kg for pts < 10 kg
  - 1.5 mg for pts 10-20 kg
  - 2.5 mg for pts 21-30 kg
  - 4 mg for pts 31-44 kg

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)

COPD Agents

- It is estimated that 16.4 million Americans have a COPD diagnosis
- COPD is a disease state 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
- Prior to 2017, patient groups were categorized into an alphabetic (ABCD) classification system based on exacerbation risk and symptoms in combination with airway limitation
- Patients are now classified separately by both their GOLD severity and exacerbation/symptom assessment

COPD Agents

2023 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

2023 GOLD Guidelines	
Assessment of Exacerbation Risk and Symptoms	
Patient Group A	Low Risk, Less Symptoms: 0 to 1 exacerbations per year (not leading to hospitalization); and CAT score < 10 or mMRC grade 0 to 1
Patient Group B	Low Risk, Less Symptoms: 0 to 1 exacerbations 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 or anticholinergic and the combination of short-acting inhaled beta2-agonist 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 ICS/LAMA/LABA can be considered for patients with eosinophils ≥ 300 cells/µL

COPD Agents

- Bronchodilator medications are central to the symptomatic management of COPD
- Act to improve emptying of the lungs, reduce dynamic hyperinflation at rest and during exercise, and improve exercise performance
- Are given either on an as-needed basis for relief of persistent or worsening symptoms or on a regular basis to prevent or reduce symptoms
- 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 agent over another

COPD Agents

Product Update:

- Ohtuvayre (ensifentrine) is a first-in-class selective dual inhibitor of phosphodiesterase 3 (PDE-3) and PDE-4 for maintenance treatment of COPD in adults.
- Ohtuvayre is an inhalation suspension available in 3mg/2.5mL ampules.
- The recommended dose is 3mg twice daily by oral inhalation using a standard jet nebulizer with a mouthpiece.
- Most common adverse reactions include back pain, hypertension, urinary tract infection, and diarrhea.

Cytokine and CAM Antagonists

ARIZONA HEALTH CARE COST CONTAINMENT SYSTEM

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	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)	--
adalimumab-aaty (Yuflyma®)	Celltrion	X	X (≥ 2 years)	X	X	X	X (≥ 6 years)	X (adults only)	**HS (adults only)**
adalimumab-adaz (Hyrimoz®)	Sandoz	X	X (≥ 2 years)	X	X	X	X (≥ 6 years)	X (adults only)	**HS (adults only)**
adalimumab-adbm (Cyltezo®)	Boehringer Ingelheim	X	X (≥ 2 years)	X	X	X	X (≥ 6 years)	X (adults only)	**HS (adults only) Uveitis (adults only)**
adalimumab-aqvh (Yusimry™)	Coherus	X	X (≥ 2 years)	X	X	X	X (≥ 6 years)	X (adults only)	**HS (adults only)**
adalimumab-atto (Amjevita™)	Amgen	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®)	Mylan Specialty	X	X (≥ 2 years)	X	X	X	X (6 years)	X (adults only)	**HS (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	--	--	--
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)**	**--**

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									
infliximab-dyyb (Zymfentra™)	Celltrion	--	--	--	--	--	X	X	--
abatacept (Orencia®)	Bristol-Myers Squibb	X	X (≥ 6 years: IV) (≥ 2 years: SC)	--	--	X	--	--	**Graft versus Host Disease (GVHD)**
anakinra (Kineret®)	Sobi-Swedish Orphan Biovitrum	X	--	--	--	--	--	--	**Cryopyrin-Associated Periodic Syndromes (CAPS)** **Deficiency of Interleukin-1 Receptor Antagonist (DIRA)**
brodalumab (Siliq®)	Bausch	--	--	--	X	--	--	--	--
canakinumab (Ilaris®)	Novartis	--	X Still's Disease and Systemic JIA (≥ 2 years)	--	--	--	--	--	**Periodic Fever syndromes, including CAPS, Tumor Necrosis Factor Receptor-Associated Periodic Syndrome (TRAPS), Hyperimmunoglobulin D Syndrome (HIDS)/ Mevalonate Kinase Deficiency (MKD), and Familial Mediterranean Fever (FMF)**
guselkumab (Tremfya®)	Janssen Biotech	--	--	--	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	MFR	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)									
rilonacept (Arcalyst®)	Kiniksa	--	--	--	--	--	--	--	**Periodic Fever syndromes: CAPS, Familial Cold Autoinflammatory Syndrome (FCAS), and Muckle-Wells syndrome (MWS)** **DIRA** **Recurrent pericarditis**
risankizumab-rzaa (Skyrizi®)	Abbvie	--	--	--	X	X	X	--	--
sarilumab (Kevzara®)	Sanofi-Aventis	X	--	--	--	--	--	--	**Polymyalgia rheumatica (PMR)**
satralizumab-mwge (Enspryng®)	Genentech	--	--	--	--	--	--	--	**NMOSD**
secukinumab (Cosentyx®)	Novartis	--	--	X	X (≥ 6 years)	X (≥ 2 years)	--	--	**nr-axSpA** **Enthesitis-related arthritis**
spesolimab-sbzo (Spevigo®)	Boehringer Ingelheim	--	--	--	--	--	--	--	**Generalized pustular psoriasis (GPP)**
tildrakizumab-asmn (Ilumya®)	Sun	--	--	--	X	--	--	--	--
tocilizumab (Actemra®)	Genentech	X	X (≥ 2 years)	--	--	--	--	--	**Giant Cell Arteritis (GCA)** **Systemic Sclerosis-Associated Interstitial Lung Disease (SSc-ILD)**
ustekinumab (Stelara®)	Janssen Biotech	--	--	--	X (≥ 6 years)	X (≥ 6 years)	X	X	--
vedolizumab (Entyvio®)	**Takeda**	--	--	--	--	--	**X**	**X**	--

Cytokine and CAM Antagonists

Drug	MFR	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	X	--	--	Oral ulcers associated with Behçet's disease
baricitinib (Olumiant®)	Eli Lilly	X	--	--	--	--	--	--	Alopecia areata
deucravacitinib (Sotyktu™)	Bristol-Myers Squibb	--	--	--	X	--	--	--	--
tofacitinib (Xeljanz®, Xeljanz XR)	Pfizer	X	X (≥ 2 years)	X	--	X	--	X	--
upadacitinib (Rinvoq®)	Abbvie	X	--	X	--	X	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, psoriatic arthritis, Crohn's disease, ankylosing spondylitis (AS), idiopathic Juvenile Arthritis (JIA), Adult-Onset Still's Disease (AOSD), and nonradiographic axial spondylarthritis (nr-axSpA), as well as other disease states
- For many disease states, including rheumatoid arthritis there is no evidence for using one tumor necrosis factor (TNF) antagonist over another
- There is no evidence that any one TNF antagonist is more effective than any other for the treatment of RA or AS
- In general, there is no indication of a specific 'first choice' for treatment in many of the targeted diseases so secondary indicators such as adverse reactions and cost may be considered
- Many of the guideline documents do not include some of the newer agents

Cytokine and CAM Antagonists

Product Update:

- FDA approved a new indication for Kevzara (sarilumab) for treatment of active polyarticular juvenile idiopathic arthritis (pJIA) in patients weighing ≥ 63 kg.
- Recommended dosage for this new indication is 200 mg SC every 2 weeks as monotherapy or in combo with conventional DMARDs.
- This dosage can be achieved with the 200 mg/1.14 mL prefilled syringe.
- Kevzara is not approved in peds < 63 kg due to lack of an appropriate dosage form.
- Live vaccines warning in PI has also been updated to state that it is recommended for pts to be brought up to date with all immunizations according to current guidelines prior to initiation of treatment.

Cytokine and CAM Antagonists

Product Update:

- FDA approved new indication for Skyrizi (risankizumab-rzaa) for treatment of moderately to severely active ulcerative colitis in adults.
- The recommended induction dosage is 1,200 mg IV infusion over ≥ 2 hours at weeks 0, 4, and 8.
- Recommended maintenance dosage is 180 mg or 360 mg SC at week 12, and every 8 weeks thereafter.

Cytokine and CAM Antagonists

Product Update:

- FDA approved interchangeable biosimilar to ustekinumab (Stelara).
- Carries all indications as Stelara, a human interleukin (IL)-12 and IL-23 antagonist, including PSO, PsA, CD, UC in adults and PSO and PsA in pediatric patients.
- Approved as 45 mg/0.5 mL and 90 mg/mL pre-filled syringes for SC injection and 130 mg/26 mL (5 mg/mL) single-dose vial for IV infusion.

Cytokine and CAM Antagonists

Product Update:

- Tofidence (tocilizumab-bavi), a biosimilar to Actemra (tocilizumab), has been approved for the following indications:
  - (1) Adults with giant cell arteritis (GCA), and
  - (2) Hospitalized adults with COVID-19 who are receiving systemic corticosteroids & require supplemental oxygen, non-invasive or invasive mechanical ventilation, or extracorporeal membrane oxygenation (ECMO).
- This product also carries indications for RA (adults), polyarticular juvenile idiopathic arthritis (pts ≥ 2 yo), & systemic juvenile idiopathic arthritis (pts ≥ 2 yo).
- When used for GCA, the recommended dosage is 6 mg/kg IV every 4 weeks in combo with tapering course of glucocorticoids; Tofidence can be used alone after discontinuation of glucocorticoids.
- For COVID-19, the recommended dosage is 8 mg/kg IV for one dose; if signs or symptoms worsen or do not improve, one additional dose may be given at least 8 hours after the initial dose.

Cytokine and CAM Antagonists

Product Update:

- The FDA approved deuruxolitinib (Leqselvi), a JAK inhibitor, for the treatment of adults with severe alopecia areata.
- It is not recommended for use in combo with other JAK inhibitors, biologic immunomodulators, cyclosporine or other potent immunosuppressants.
- Supplied as an 8 mg oral tablet.
- Recommended dosage is 8 mg twice daily.
- Boxed warning for serious infections, mortality, malignancy, MACE, and thrombosis.

Cytokine and CAM Antagonists

Product Update:

- FDA approved Amjetiva (adalimumab-atto) as interchangeable to adalimumab (Humira) for SC use as:
  - Amjevita 10 mg/0.2 mL in a prefilled syringe (PFS) as interchangeable with Humira 10 mg/0.2 mL in a PFS
  - Amjevita 20 mg/0.4 mL in a PFS as interchangeable with Humira 20 mg/0.4 mL in a PFS
  - Amjevita 40 mg/0.8 mL in a PFS as interchangeable with Humira 40 mg/0.8 mL in a PFS
  - Amjevita 40 mg/0.8 mL in a prefilled autoinjector as interchangeable with Humira 40 mg/0.8 mL in a prefilled pen.

Cytokine and CAM Antagonists

Product Update:

- Cimzia (certolizumab pegol) is now approved for the treatment of active polyarticular Juvenile Idiopathic Arthritis (pJIA) for patients 2 years of age and older.
- The recommended dosage for pJIA is based on body weight with a loading dose given at week 0, 2, and 4 followed by maintenance doses beginning at week 6 and given every 2 weeks thereafter.
- The doses range from 50 mg every 2 weeks to 400 mg loading doses.
- There is not a dosage form that allows for patient self-administration < 200 mg, doses < 200 mg require HCP administration using the vial kit.

Cytokine and CAM Antagonists

Product Update:

- FDA approved Ebglyss (lebrikizumab-lbkz), an IL-13 antagonist indicated for the treatment of adults and pediatric patients 12 years of age and older who weigh at least 40 kg with moderate to severe atopic dermatitis whose disease is not adequately controlled with topical prescription therapies are not advisable.
- Ebglyss can be used with or without topical corticosteroids, topical calcineurin inhibitors can be used but reserved for sensitive areas only.
- Ebglyss will be supplied in 250mg/2mL single-dose prefilled pen and prefilled syringe with needle shield.
- The recommended dosage is 500 mg (two 250 mg injections) at week 0 and week 2, followed by 250 mg (one injection) every 2 weeks until week 16 or later, when adequate clinical response is achieved.
- The maintenance dose is 250 mg every 4 weeks.
- Ebglyss is administered subcutaneously in the abdomen, thigh, or back of upper arm (by a caregiver or HCP). There most common adverse reactions were conjunctivitis, injection site reactions, and herpes zoster.

Cytokine and CAM Antagonists

Product Update:

- Bimzelx (bimekizumab-bkzx) received new FDA approved new indications for:
  - (1) Adults with active psoriatic arthritis (PsA)
  - (2) Adults with active ankylosing spondylitis (AS), and
  - (3) Adults with active non-radiographic axial spondyloarthritis (nr-axSpA) with objective signs of inflammation.
- Recommended dosage for all 3 new indications is 160 mg SC every 4 weeks.
  - If pt has coexisting PsA and PSO, use dosage for PSO.

Cytokine and CAM Antagonists

Product Update:

- FDA approved Tremfya (guselkumab) for treatment of adults with moderately to severely active ulcerative colitis (UC).
- For UC, Tremfya is administered as a 200 mg IV induction dose at weeks 0, 4, & 8 by an HCP; recommended maintenance dosage is 100 mg SC at week 16 and every 8 weeks thereafter, or 200 mg SC at week 12 and every 4 weeks thereafter.
- Maintenance doses can be administered by the pt or a caregiver.
- The lowest effective dosage should be used to maintain therapeutic response.
- Tremfya is also already approved for treatment of select adults with plaque psoriasis or active psoriatic arthritis.

Cytokine and CAM Antagonists

Product Update:

- FDA approved ustekinumab-aauz (Otulfi) as biosimilar to ustekinumab (Stelara).
- This human interleukin (IL)-12 and IL-23 antagonist carries all of the same indications as Stelara, including PsO, PsA, CD, & UC in adults and PSO & PsA in peds ≥ 6 yo.
- Approved as 45 mg/0.5 mL & 90 mg/mL pre-filled syringes for SC injection and 130 mg/26 mL (5 mg/mL) SDV for IV infusion.

Cytokine and CAM Antagonists

Product Update:

- FDA approved ustekinumab-srlf (Imuldosa) as biosimilar to ustekinumab (Stelara).
- This human interleukin (IL)-12 and IL-23 antagonist carries all of the same indications as Stelara, including PsO, PsA, CD, & UC in adults and PSO & PsA in peds ≥ 6 yo.
- Approved as 45 mg/0.5 mL & 90 mg/mL PFS for SC injection and 130 mg/26 mL (5 mg/mL) SDV for IV infusion.

Cytokine and CAM Antagonists

Product Update:

- Two new 2 mL device presentations of bimekizumab-bkzx (Bimzelx) have been approved; a 320 mg/2 mL (160 mg/mL) single-dose prefilled autoinjector & a 320 mg/2 mL (160 mg/mL) single-dose PFS.

Cytokine and CAM Antagonists

Product Update:

- FDA approved a new indication for Selarsdi for moderately to severely active CD and moderately to severely active UC in adults.
- FDA also approved a 130 mg/26 mL vial.
- FDA also approved an unbranded version of ustekinumab-aekn, by Teva, for the same indications, route of administration (IV, SC) and presentations as Selarsdi and Stelara.

Cytokine and CAM Antagonists

Product Update:

- Bimzelx (bimekizumab-bkzx) is now approved for the treatment of adults with moderate to severe hidradenitis suppurativa (HS).
- The recommending dose for this new indication is 320 mg subcutaneously at weeks 0, 2, 4, 6, 8, 10, 12, 14, and 16, then every 4 weeks thereafter.

Cytokine and CAM Antagonists

Product Update:

- FDA approved Yesintek (Ustekinumab-kfce) as biosimilar to the human interleukin-12 and -23 antagonist ustekinumab (Stelara).
- Yesintek carries the same indications as Stelara
  - Which are for use in adults with:
    - (1) Moderate to severe PSO who are candidates for phototherapy or systemic therapy
    - (2) Active PsA
    - (3) Moderately to severely active Crohn's disease (CD)
    - (4) Moderately to severely active UC
  - For use in pediatric patients ≥6 yo with:
    - (1) moderate to severe PSO, who are candidates for phototherapy or systemic therapy.
    - (2) active PsA
- Yesintek is approved as 45 mg/0.5 mL or 90 mg/mL soln in single-dose PFS for SC admin and 130 mg/26 mL single-dose vial for IV administration.

Cytokine and CAM Antagonists

Product Update:

- Boehringer Ingelheim has discontinued adalimumab-adbm (unbranded version of Cyltezo) 40 mg/0.8 mL prefilled pen starter package for psoriasis/uveitis and adalimumab-adbm 40 mg/0.8 mL prefilled pen starter package for CD/UC/HS.
- All other formulations of both Cyltezo & unbranded adalimumab-adbm remain available.

Cytokine and CAM Antagonists

Product Update:

- Pyzchiva (ustekinumab-ttwe) is now available in a 45 mg/0.5 mL single-dose vial for SC injection.
- This was added to the PI as biosimilar to Stelara 45 mg/0.5 mL vial for SC use.
- This presentation was developed to accurately administer drug to pediatric patients weighing < 60 kg.

Cytokine and CAM Antagonists

Product Update:

- Wezlana (ustekinumab-auub) is available in 45 mg/0.5 mL & 90 mg/mL solution single-dose prefilled ConfiPen autoinjector presentations.
- These autoinjector pens are for SC injection and are biosimilar to Stelara 45 mg/0.5 mL & 90 mg/mL single-dose PFS, respectively.

Cytokine and CAM Antagonists

Product Update:

- All strengths of Boehringer-Ingelheim's Cyltezo injection kits, and the unbranded versions, were discontinued as of January 6, 2025.

Cytokine and CAM Antagonists

Product Update:

- FDA has approved Omvoh (mirikizumab-mrkz) for the treatment of mod-to-severely active Crohn's disease (CD) in adults.
- Previously, the IL-23 antagonist was indicated only for mod-to-severely active ulcerative colitis in adults.
- Dosing for CD is initiated as an induction regimen of 900 mg IV over ≥ 90 mins at week 0, week 4 & week 8, followed by 300 mg given as a SC maintenance dosage starting at week 12 & given every 4 weeks thereafter.

Cytokine and CAM Antagonists

Guideline Update:

- American College of Gastroenterology published guidelines for the diagnosis and management of eosinophilic esophagitis (EoE).
- Recommend diagnosis of EoE is based on the presence of symptoms of esophageal dysfunction and ≥ 15 eosinophils per high-power field on esophageal biopsy.
- PPIs are suggested and swallowed topical steroids are recommended as a treatment.
- Use of either fluticasone propionate or budesonide is suggested for pts with EoE treated with topical steroids.
- An empiric food elimination diet is suggested for EoE treatment, but currently available allergy testing to direct food elimination diets is not suggested.
- Dupilumab is suggested for individuals aged ≥12 years & for peds pts who are nonresponsive to PPI therapy.
- Omalizumab is not suggested for EoE treatment.
- For esophageal strictures causing dysphagia, endoscopic dilation is suggested as an adjunct to medical therapy.

Cytokine and CAM Antagonists

Product Update:

- FDA has approved tocilizumab-anoh (Avtozma), a biosimilar to tocilizumab (Actemra).
- The IL-6 receptor antagonist is indicated for adults with
  - (1) Mod-severely active RA who have had an inadequate response to ≥ 1 DMARDs
  - (2) Adults with giant cell arteritis
  - (3) Hospitalized adults with COVID-19 who are receiving systemic corticosteroids & require supplemental oxygen, non-invasive or invasive mechanical ventilation, or ECMO.
- It is also indicated for pts ≥ 2 yo with
  - (1) Active polyarticular juvenile idiopathic arthritis
  - (2) Active systemic juvenile idiopathic arthritis.
- Product is approved in both an IV formulation (80 mg/4 mL, 200 mg/10 mL, 400 mg/20 mL in SDVs for further dilution prior to IV infusion) and SC formulation (162 mg/0.9 mL in a single-dose PFS or single-dose prefilled autoinjector).

Cytokine and CAM Antagonists

Product Update:

- Otulfi (ustekinumab-aauz) PI updated to align with labeling changes for reference product Stelara.

Cytokine and CAM Antagonists

Product Update:

- FDA approved an 80 mg/0.8 mL single-dose autoinjector for Simlandi (adalimumab-ryvk).
- Previously approved as:
  - 40mg/0.4 mL autoinjector and 80 mg/0.8 mL
  - 40 mg/0.4 mL
  - 20 mg/0.2 mL prefilled syringes

Cytokine and CAM Antagonists

Product Update:

- Tyenne (tocilizumab-aazg) is now approved for
  - (1) Adults & peds ≥ 2 years of age with CAR T-cell induced severe or life-threatening cytokine release syndrome (CRS)
  - (2) Hospitalized adults with COVID-19 who are receiving systemic corticosteroids & require supplemental oxygen, non-invasive or invasive mechanical ventilation, or extracorporeal membrane oxygenation (ECMO).
- When used for CRS, Tyenne should be given as a 60-minute IV infusion at a dose of 12 mg/kg for patients weighing < 30 kg & 8 mg/kg for patients weighing ≥ 30 kg; up to 3 additional doses can be given if no clinical improvement is seen after the first dose.
- For COVID-19, the recommended dosage is 8 mg/kg IV as a single 60-minute infusion; one additional dose can be given after ≥ 8 hours if clinical signs or symptoms worsen or do not improve after the first dose.
- Doses > 800 mg per infusion are not recommended for either new indication, and SC administration is not approved for either new indication.

Cytokine and CAM Antagonists

Product Update:

- Tremfya (guselkumab) is now approved for the treatment of adults with moderately to severely active Crohn's disease.
- The recommended dosage is an induction course of 200 mg via IV infusion over ≥ 1 hr or 400 mg via SC injection given at week 0, week 4 and week 8.
- The recommended maintenance dosage is 100 mg SC at week 16, and every 8 weeks thereafter or 200 mg SC at week 12, and every 4 weeks thereafter.
- The lowest effective recommended dosage that maintains therapeutic response should be used.
- FDA approved a single-dose prefilled pen (autoinjector) in the strength of 100 mg/mL for SC use.

Cytokine and CAM Antagonists

Product Update:

- Uplizna (inebilizumab-cdon) has been approved as the first & only tx for immunoglobulin G4-related disease (IgG4-RD) in adults.
- Recommended dosage for this new indication is the same as for existing indication for neuromyelitis optica spectrum disorder (NMOSD)
  - Initial dose is 300 mg IV followed 2 weeks later by a second 300 mg IV infusion
  - Subsequent doses starting 6 months after the first infusion should be given as single 300 mg IV infusions every 6 months.

Cytokine and CAM Antagonists

Product Update:

- FDA approved the following presentations of Simlandi (adalimumab-ryvk) for SC inj. as interchangeable to corresponding Humira presentations: 80 mg/0.8 mL prefilled syringe & autoinjectors and the 20 mg/0.2mL prefilled syringes.

Cytokine and CAM Antagonists

Product Update:

- FDA approved an unbranded labeling for Otulfi (ustekinumab-aauz), 45 mg/0.5 mL and 90 mg/mL pre-filled syringe, and 45 mg/0.5 mL and 130 mg/26 mL single-dose vial.

Cytokine and CAM Antagonists

Product Update:

- FDA approved Dupixent (dupilumab) for treatment of patients ≥ 12 yo with chronic spontaneous urticaria (CSU) who remain symptomatic despite histamine-1 (H1) antihistamine treatment.
- It is not indicated for other forms of urticaria.
- Recommended dosage:
  - In adults and patients 12-17 yo weighing ≥ 60 kg with CSU is an initial dose of 600 mg (two 300 mg SC injections) followed by 300 mg every 2 weeks.
  - In patients 12-17 yo weighing 30 kg to < 60 kg is 400 mg (two 200 mg SC inj) for first dose, then 200 mg every 2 weeks thereafter.

Cytokine and CAM Antagonists

Product Update:

- FDA approved the following presentations as interchangeable to corresponding Humira (adalimumab-atto) presentations: 80 mg/0.8 mL prefilled syringe & autoinjectors and the 20 mg/0.2mL prefilled syringes.

Glucagon Agents

ARIZONA HEALTH CARE COST CONTAINMENT SYSTEM

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 2024 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

Glucocorticoids, Inhaled

ARIZONA HEALTH CARE COST CONTAINMENT SYSTEM

Glucocorticoids, Inhaled

Class Overview: Single Agent Glucocorticoid Products

- beclomethasone HFA - (QVAR RediHaler)
- budesonide powder - (Pulmicort FlexHaler)
- budesonide solution - (Pulmicort Respules)
- ciclesonide aerosol - (Alvesco)
- fluticasone furoate powder – (Arnuity Ellipta)
- fluticasone propionate aerosol – (Flovent HFA)
- fluticasone propionate powder – (ArmonAir Digihaler, Flovent Diskus)
- mometasone furoate aerosol – (Asmanex HFA)
- mometasone furoate powder – (Asmanex Twisthaler)

Glucocorticoids, Inhaled

Class Overview: Glucocorticoid/Long-Acting Beta$_2$ (LABA) Combination Products

- budesonide/formoterol aerosol - (Symbicort)
- fluticasone furoate/vilanterol powder - (Breo Ellipta)
- fluticasone propionate/salmeterol aerosol - (Advair HFA)
- fluticasone propionate/salmeterol powder - (Advair Diskus, AirDuo RespiClick, AirDuo RespiClick)
- mometasone/formoterol aerosol - (Dulera)

Glucocorticoids, Inhaled

Class Overview: Glucocorticoid/Long-Acting Anticholinergic/Long-Acting Beta$_2$ (LABA) Combination Products

- budesonide/glycopyrrolate/ formoterol fumarate- (Breztri Aerosphere)
- fluticasone furoate/umeclidinium/vilanterol powder - (Trelegy Ellipta)

Glucocorticoids, Inhaled

- Prevalence of asthma in the United States (US) continues to rise
  - More than 25 million Americans have asthma, and over 4 million of these are children

- The National Asthma Education and Prevention Program (NAEPP) has defined asthma as a chronic inflammatory disorder of the airways in which many cells and cellular elements play a role
  - In susceptible individuals, inflammation may cause recurrent episodes of wheezing, breathlessness, chest tightness, and coughing
  - These episodes are usually associated with airflow obstruction that is often reversible, either spontaneously or with treatment
  - The inflammation also causes an increase in bronchial hyper-responsiveness to a variety of stimuli

- Studies have demonstrated the efficacy of inhaled corticosteroids (ICS) in improving lung function, reducing symptoms, reducing frequency and severity of exacerbations, and improving the quality of life (QoL) of patients with asthma
  - The 2007 National Heart, Lung, and Blood Institute (NHLBI) states that inhaled glucocorticoids are currently the most effective anti-inflammatory medications for the treatment of persistent asthma
  - The 2019 GINA full report advises that all patients with asthma should receive ICS-containing controller treatment to reduce risk of serious exacerbations and to control symptoms

Glucocorticoids, Inhaled

Global Initiative for Asthma (GINA), 2024

- The guidelines offer a control-based management plan to adjust treatment in a continuous cycle of assessment, treatment, and review of the patient's response as it relates to symptom control, future risk of exacerbations, and side effects
- Equally important in this process is identifying the patient's own goals regarding their asthma management to ensure improved outcomes
- In patients whose asthma is not adequately controlled on the preferred controller despite good adherence and correct technique, a step up in treatment may be added until control is achieved. This can be a short-term or sustained step up in therapy. If control is maintained for at least 3 months on the current regimen, treatment can be stepped down to the lowest step and dosage that maintains control
- Patients should be started on treatment based on symptoms, with infrequent symptoms beginning at Step 1 and patients with the most frequent, severe, or debilitating symptoms beginning at Step 4
- Notably, reliever therapy can be considered for symptom management prior to exercise, if needed
- The GINA 2021 guidelines describe 2 treatment tracks: Track 1 and Track 2 (next slide)
    - In Track 1, the reliever is as-needed low dose ICS-formoterol
    - In Track 2, the reliever is an as-needed SABA, which is the alternative approach when Track 1 is not an option or is not preferred for patient-specific reasons

Glucocorticoids, Inhaled

Global Initiative for Asthma (GINA), 2024

Step	Track 1	Track 2	Other Controller Options
1	▪ As-needed low dose ICS/formoterol	▪ Low dose ICS (whenever SABA is taken) ▪ **With as-needed ICS-SABA or as-needed SABA**	--
2	▪ **As-needed low dose ICS/formoterol**	▪ **Low dose maintenance ICS** ▪ **With as-needed ICS-SABA** or as needed SABA	▪ Low dose ICS (whenever SABA is taken) or daily LTRA or add HDM SLIT
3	▪ Low dose maintenance ICS/formoterol ▪ With as-needed low dose ICS/formoterol	▪ Low dose maintenance ICS/LABA ▪ **With as-needed ICS-SABA** or as needed SABA	▪ Medium dose ICS or add LTRA or add HDM SLIT
4	▪ Medium dose maintenance ICS/formoterol ▪ With as-needed low dose ICS/formoterol	▪ **Medium/high dose maintenance ICS/LABA** ▪ **With as-needed ICS-SABA** or as needed SABA	▪ Add LAMA or add LTRA or erlizumab **HDM SLIT** or switch to high dose ICS
5	▪ **Add on LAMA**; refer for phenotypic assessment ± anti-IgE (omalizumab), anti-IL-5/5R (mepolizumab, reslizumab, benralizumab), anti-IL4R (dupilumab), **anti-TSLP (tezepelumab)** ▪ **Consider high dose ICS/formoterol** ▪ With as-needed low dose ICS/formoterol	▪ **Add on LAMA;** refer for phenotypic assessment ± anti-IgE (omalizumab), anti-IL-5/5R (mepolizumab, reslizumab, benralizumab), anti-IL4R (dupilumab) ▪ **Consider high dose ICS/LABA ± anti-IgE (omalizumab), anti-IL-5/5R (mepolizumab, reslizumab, benralizumab), anti-IL4R (dupilumab), anti-TSLP (tezepelumab)** ▪ **With as-needed ICS-SABA or as-needed SABA**	▪ Add azithromycin (adults) or add LTRA or add low dose oral corticosteroid (considering adverse effects)

Glucocorticoids, Inhaled

- In asthma therapy, corticosteroids suppress cytokine generation, recruitment of airway eosinophils, and release of inflammatory mediators, reducing airway hyper-responsiveness.
- LABAs lead to bronchial relaxation and a decrease in the release of mediators of immediate hypersensitivity from mast cells.
- LAMAs antagonize the action of released acetylcholine causing bronchodilation.
- Delivery system selection as well as the patients' ability to properly use the device are important factors in the clinical success of ICS therapy.
- Metered dose inhalers (MDIs) are pressurized spray inhalers, available in suspension and solution.

Glucocorticoids, Inhaled

- MDIs deliver approximately 15% to 35% of the administered dose to the lungs
- Spacer chambers may be used with most MDIs to make them easier to use and help deliver a greater drug amount to the airway
- Products in this review with MDI devices include Advair HFA, Alvesco, Asmanex HFA, Dulera, Flovent HFA, QVAR Redihaler, Symbicort, and Breztri Aerosphere.
- QVAR Redihaler differs from conventional MDIs as it is breath activated, and should not be used with a spacer or volume holding chamber
- Dry-powder inhalers (DPIs) are breath-actuated devices that release the drug in the form of a dry powder upon inhalation

Glucocorticoids, Inhaled

- While DPIs minimize some of the difficulties in coordinating MDI usage, they have a tendency to result in more dosage variation at low inspiratory flow rates (< 20 L/min).
- Products in this review with DPI devices include Advair Diskus, AirDuo RespiClick, AirDuo Digihaler, Arnuity Ellipta, ArmonAir Digihaler, Asmanex Twisthaler, Breo Ellipta, Flovent Diskus, Pulmicort Flexhaler, and Trelegy Ellipta.
- Products in this review that are nebulized include budesonide and Pulmicort respules.
- Several of the products listed also carry indications in the treatment of COPD.

Glucocorticoids, Inhaled

- When used in equivalent dosages, efficacy among all ICS is similar.
- There are differences among the agents in dosage frequency and the number of inhalations needed for each dose. Most are recommended for twice daily use.
- Arnuity Ellipta, Breo Ellipta, Trelegy Ellipta and Asmanex Twisthaler can be dosed once daily.
- Alvesco and QVAR Redihaler are either converted during absorption (beclomethasone) or in the lung (ciclesonide).
- FDA cautions on the use of LABA products in asthma, as well as the combination ICS/LABA products but the latter no longer carry a boxed warning.
- The FDA recommends against the use of LABA without the use of an ICS, and for the shortest duration possible to maintain asthma control.

Glucocorticoids, Inhaled

Product/Guideline Updates:

- Teva discontinued the manufacture of AirDuo Digihaler (fluticasone/salmeterol) 55 mcg/14 mcg, 113 mcg/14 mcg; & 232 mcg/14 mcg metered powder inhaler.

Glucocorticoids, Inhaled

Product/Guideline Updates:

- Teva discontinued the manufacture of ArmonAir Digihaler (fluticasone) 55 mcg, 113 mcg, & 232 mcg metered powder inhaler.

Growth Hormone

ARIZONA HEALTH CARE COST CONTAINMENT SYSTEM

Growth Hormone

Class Overview: Products

- Genotropin cartridge & syringe (somatropin)
- Humatrope cartridge & vial (somatropin)
- Ngenla (somatrogon-ghla)
- Norditropin pens (somatropin)
- Nutropin AQ NuSpin cartridge (somatropin)
- Omnitrope cartridge & vial (somatropin)
- Saizen cartridge & 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
- 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

Growth Hormone

- 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)
- Several products carry an indication for Turner Syndrome: Genotropin; Humatrope; Norditropin; Nutropin AQ; Omnitrope; Zomacton

Growth Hormone

- 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 to increase lean body mass and weight, and improve physical endurance
- Zorbtive is indicated for Short Bowel Syndrome

Growth Hormone

Product/Guideline Updates:

- Eli Lilly made a business decision to discontinue Humatrope.
- Distribution will continue through 2026.
- There are no generic alternatives available

Hepatitis C Agents Direct Acting

ARIZONA HEALTH CARE COST CONTAINMENT SYSTEM

Hepatitis C Agents (Direct Acting)

Class Overview: Products – Direct Acting Agents

- Oral Combination Products
  - elbasvir/grazoprevir – (Zepatier)
  - glecaprevir/pirbrentasvir – (Mavyret)
  - ledipasvir/sofosbuvir – (Harvoni)
  - sofosbuvir/velpatasvir – (Epclusa)
  - sofosbuvir/velpatasvir/voxilaprevir – (Vosevi)

Hepatitis C Agents (Direct Acting)

Class Overview: Products – Direct Acting Agents

- Oral NS5B Polymerase Inhibitor
    - sofosbuvir – (Sovaldi)

Hepatitis C Agents (Direct Acting)

- Approximately 2.7 million people in the US 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 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 recommended regimens (favored for most patients) and alternative regimens (optimal in a particular subset of patients).

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/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 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

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®)	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
semaglutide (Rybelsus®)	Novo Nordisk	▪ Adjunct to diet and exercise to improve glycemic control in adults with T2DM
Glucose-dependent Insulinotropic Polypeptide (GIP) Receptor Agonist/GLP-1RA		
tirzepatide (Mounjaro®)	Eli Lilly	▪ Adjunct to diet and exercise to improve glycemic control in adults with T2DM

Hypoglycemics, Incretin Mimetics/Enhancers

- It is estimated that over 37 million people in the US have diabetes.
- Type 2 diabetes (T2DM) accounts for over 96% of all diagnosed cases of diabetes
- Per the ADA 2023 Standards of Medical Care in Diabetes, metformin, if not contraindicated and if tolerated, is a first-line option, in addition to lifestyle management, in the treatment of T2DM
- In patients with T2DM with or at high risk for atherosclerotic cardiovascular disease (ASCVD), heart failure (HF), and/or chronic kidney disease (CKD), GLP-1RAs and SGLT2 inhibitors, with or without metformin based on glycemic needs, are appropriate independent of HbA1c as initial or add-on therapy
- The ADA discusses the importance of weight management as a component of glucose-lowering treatment for T2DM; GLP-1RAs and SGLT2 inhibitors are preferred when increased body weight is a concern

Hypoglycemics, Incretin Mimetics/Enhancers

- The 2022 American Association of Clinical Endocrinology (AACE) updated guidelines contain the following recommendations:
  - Metformin as preferred initial therapy, in general
  - GLP-1RAs and SGLT2 inhibitors with proven CV benefits for patients with established ASCVD or who are at high risk for ASCVD
  - Pioglitazone for patients with T2DM and prior stroke or transient ischemic attack
  - SGLT2 inhibitors for T2DM patients with established HF
  - GLP-1RAs or SGLT2 inhibitors for patients with obesity

Hypoglycemics, Incretin Mimetics/Enhancers

- Per the 2022 Kidney Disease Improving Global Outcomes (KDIGO) guidelines on managing patients with diabetes and CKD:
  - First-line treatment with metformin in most patients with estimated glomerular filtration rate (eGFR) ≥ 30 mL/min/1.73 m2
  - first-line treatment with a SGLT2 inhibitor in most patients with an eGFR ≥ 20 mL/min/1.73 m2
  - A long-acting GLP-1RA for patients who do not achieve their target HbA1c despite use of metformin and an SGLT2 inhibitor
  - DPP-4 inhibitors, insulin, SUs, TZDs, and/or alpha-glucosidase inhibitors (AGI) may be added for glycemic control, as needed
  - Use of a GLP-1RA with a DPP-4 inhibitor is not recommended

Hypoglycemics, Incretin Mimetics/Enhancers

- The American Gastroenterological Association (AGA) estimates that up to 70% of individuals with T2DM have nonalcoholic fatty liver disease (NAFLD)
- They made the following statements in their 2021 guidance:
  - GLP-1RAs, SGLT2 inhibitors, and pioglitazone can improve the cardiometabolic profile and reverse steatosis in patients with diabetes and NAFLD
  - A GLP-1RA or pioglitazone is recommended in patients with indeterminate or high risk clinically significant liver fibrosis.
  - SLGT2 inhibitors appear to provide benefit in patients with nonalcoholic steatohepatitis (NASH) and associated comorbidities
  - Prescribing GLP-1RAs and SGLT2 inhibitors is advised according to the ADA guidelines.

Hypoglycemics, Incretin Mimetics/Enhancers

- According to the 2020 AACE and the American College of Endocrinology (ACE) updated algorithm for the management of T2DM:
  - Metformin is the preferred treatment of choice for monotherapy and a first-line agent for dual and triple therapy.
  - GLP-1RAs and SGLT2 inhibitors with proven ASCVD and/or CKD benefits may be preferred, including use as first-line treatment, in patients with those complications
  - Liraglutide, empagliflozin, dapagliflozin, and canagliflozin may offer renal and CV benefits
  - Data for semaglutide and dulaglutide also suggest associated CV benefit.
  - Saxagliptin and alogliptin may be associated with possible CV risk
  - Possible increased risk of bone fractures with canagliflozin
  - Increased congestive heart failure risk with sulfonylureas (SU), glitinides, and insulin
  - Medications to be used with caution include thiazolidinediones (TZD) and SUs

Hypoglycemics, Incretin Mimetics/Enhancers

- In general, selection of antidiabetic medication should be based on patient-related variables, such as comorbidities, hypoglycemia risk, patient preference, as well as agent-related variables, such as its effect on body weight, adverse effect profile, and cost
- DPP-4 Enzyme Inhibitors increase insulin secretion and reduce glucagon secretion by preventing inactivation of GLP-1.
- GLP-1 Receptor Agonists enhance glucose-dependent insulin secretion, suppress elevated glucagon secretion, and slow gastric emptying.
- HbA1c improvements for Amylin Analogues average 0.3% to 0.6% with a potential weight reduction of 0.5 kg to 1.5 kg.
- HbA1c improvements for DPP-4s average 0.5% to 1%
- These agents are weight-neutral and have a low hypoglycemia risk when used as monotherapy or in conjunction with metformin.

Hypoglycemics, Incretin Mimetics/Enhancers

- GLP-1 receptor agonists are associated with the following reductions in HbA1c: dulaglutide by 0.7% to 1.6%, exenatide and liraglutide by 0.5% to 1.6%, lixisenatide by 0.3% to 0.65%, injectable semaglutide by 1.4% to 1.5%, and oral semaglutide by 1.2% to 1.4%.
- Mean reductions in HbA1c from baseline ranged from 1.87% to 2.58% with tirzepatide
- Evidence for reducing CV events for GLP-1RA has been demonstrated for liraglutide, semaglutide, and dulaglutide
- For SGLT2 inhibitors, empagliflozin, dapagliflozin, and canagliflozin have shown benefit in reducing HF and CKD progression

Hypoglycemics, Incretin Mimetics/Enhancers

The American Heart Association & American College of Cardiology (ACC), 2024

- Published updated recommendations for management of lower-extremity peripheral artery disease (PAD)
- The guideline defines 4 clinical subsets of PAD:
  - Asymptomatic PAD
  - Chronic symptomatic PAD
  - Chronic limb-threatening ischemia
  - Acute limb ischemia
- Effective treatment to prevent MACE & major adverse limb events includes antiplatelet & antithrombotic treatment, lipid-lowering & antihypertensive treatment, DM management, & smoking cessation
- The combination of rivaroxaban 2.5 mg twice daily plus aspirin 81 mg daily is recommended for patients who are not at increased risk for bleeding

United States Preventive Services Task Force (USPSTF), 2024

- Recommend pediatric patients ≥ 6 years of age with high BMI (≥95th percentile for age and sex) be referred to comprehensive intensive behavioral interventions (B recommendation)
- Effective interventions include at least 26 or more hours with an HCP over one year
- USPSTF determined evidence on weight loss medications long-term health outcomes is lacking

Hypoglycemics, Incretin Mimetics/Enhancers

The Lancet Diabetes & Endocrinology Commission, 2024

- Has published diagnostic criteria & definitions for clinical obesity
- Obesity is defined as "a condition characterized by excess adiposity, with or without abnormal distribution or function of adipose tissue, and with causes that are multifactorial and still incompletely understood"
- Clinical obesity is a "chronic, systemic illness characterized by alterations in the function of tissues, organs, the entire individual, or a combination thereof, due to excess adiposity" and can lead to severe end-organ damage as well as other complications (e.g., heart attack, stroke, and renal failure)
- Preclinical obesity is defined as "a state of excess adiposity with preserved function of other tissues and organs and a varying, but generally increased, risk of developing clinical obesity and several other non-communicable diseases (e.g., T2DM, CVD, certain cancers, mental disorders)"

Hypoglycemics, Incretin Mimetics/Enhancers

Product/Guideline Updates:

- Discontinuations
  - exenatide (Byetta)- November 2024
    - AstraZeneca has announced that it will discontinue the manufacture of Byetta 300 mcg/1.2 mL & 600 mcg/2.4 mL injection
  - exenatide (Byetta Bcise)- November 2024
    - AstraZeneca has announced that it will discontinue the manufacture of Bydureon Bcise ER 2 mg/0.85 mL injectable suspension
  - dapagliflozin/saxagliptin (Qtern)- March 2025
    - FDA reports AstraZeneca will discontinue Qtern 5 mg/5 mg & 10 mg/5 mg tablets

Hypoglycemics, Incretin Mimetics/Enhancers

Product/Guideline Updates:

- New Generics
  - exenatide- November 2024
    - FDA approved the first generic for AstraZeneca's Byetta injection from Amneal
  - liraglutide (Victoza)- December 2024
    - FDA approved the first generic for Novo Nordisk's Victoza from Hikma
    - Product will be available in an 18 mg/3 mL prefilled, single-pt-use pen that delivers 0.6 mg, 1.2 mg, & 1.8 mg doses

Hypoglycemics, Incretin Mimetics/Enhancers

Product/Guideline Updates:

- FDA approved Zituvimet XR (sitagliptin/metformin) tablets as an adjunct to diet & exercise to improve glycemic control in adults with T2DM.
  - This combo dipeptidyl peptidase-4 (DPP-4) inhibitor/biguanide product is not indicated for treatment of T1DM and has not been studied in patients with a history of pancreatitis.
- The recommended starting dose for pts who are not on metformin is 100 mg sitagliptin/1,000 mg metformin once daily, with gradual dose escalation to minimize risk of GI side effects.
  - Dosage should be individualized based on pt's current regimen and effectiveness & tolerability.
  - Max dose is 100 mg of sitagliptin & 2,000 mg of metformin per day.
- Zituvimet XR carries a boxed warning for lactic acidosis.
- Product available as sitagliptin 50 mg/metformin 500 mg ER tabs, sitagliptin 50 mg/metformin 1,000 mg ER tabs, & sitagliptin 100 mg/metformin 1,000 mg ER tabs.

Hypoglycemics, Incretin Mimetics/Enhancers

Product/Guideline Updates:

- FDA approved Brynovin (sitagliptin), a 25mg/mL oral solution formulation of sitagliptin.
- Brynovin is indicated as an adjunct to diet and exercise to improve glycemic control in adults with T2DM.
- Not recommended in T1DM and has not been studied in patients with pancreatitis.
- The recommended dose is 100 mg (4 mL) orally once daily with adjustments for patients with eGFR < 45mL/min/1.73m^2.
- Most common adverse reactions are: upper respiratory tract infection, nasopharyngitis and headache.

Hypoglycemics, Incretin Mimetics/Enhancers

Product/Guideline Updates:

- FDA approved a new indication for Ozempic (semaglutide) to reduce the risk of sustained eGFR decline, ESRD, CV death in adults with T2DM and CKD.
- Recommended dosage is consistent with other indications with 0.25 mg SC once weekly for first 4 weeks, then increase to 0.5 mg once weekly.
  - May increase to 1 mg or 2 mg once weekly based on glycemic control.
  - Max dose is 2 mg once weekly.

Hypoglycemics, Insulin and Related Agents

ARIZONA HEALTH CARE COST CONTAINMENT SYSTEM

Hypoglycemics, Insulin and Related Agents

Class Overview: Rapid-Acting Insulins

- human insulin inhalation powder - (Afrezza)
- insulin aspart - (Fiasp; Novolog)
- insulin glulisine - (Apidra)
- insulin lispro - (Admelog; Humalog; Humalog Junior)
- insulin lispro-aabc - (Lyumjev)

Class Overview: Regular Insulins

- human insulin - (Humulin R; Novolin R)

Class Overview: Intermediate Insulins

- human insulin NPH - (Humulin N; Novolin N)

Hypoglycemics, Insulin and Related Agents

Class Overview: Long-Acting Insulins

- insulin degludec - (Tresiba)
- insulin detemir - (Levemir)
- insulin glargine U-100 - (Basaglar; Lantus)
- insulin glargine-yfgn U-100 - (Semglee) – interchangeable biosimilar
- insulin glargine-aglr U-100 – (Rezvoglar) – interchangeable biosimilar
- insulin glargine U-300 - (Toujeo)

Hypoglycemics, Insulin and Related Agents

Class Overview: Rapid/Intermediate-Acting Combination Insulins

- insulin aspart 70/30 - (Novolog Mix 70/30)
- insulin lispro 50/50; 75/25 - (Humalog Mix 50/50, 75/25)

Class Overview: Regular/Intermediate-Acting Combination Insulins

- human insulin 70/30 - (Humulin 70/30; Novolin 70/30)

Hypoglycemics, Insulin and Related Agents

- Exogenous insulin supplements deficient levels and temporarily restores the body's ability to properly utilize carbohydrates, fats, and proteins
- Multiple insulin products are available and used in the management of both T1DM and T2DM
- Insulin therapy is the treatment of choice for T1DM and T2DM in pregnancy as it does not cross the placenta to a measurable degree
- All of the rapid-acting insulins except Afrezza are approved for use in pediatric patients as well as for use in external insulin pumps.

Hypoglycemics, Insulin and Related Agents

- Insulin therapy is contraindicated during episodes of hypoglycemia.
- Admelog, Basaglar, and Semglee were approved through an abbreviated approval pathway under a 505(b)(2) application
- Effective March 23, 2020, all insulin products previously approved under this pathway are now considered to be biologics under section 351 of the Public Health Service Act
- Lyumjev was approved under section 351(a) of the Public Health Service Act (PHSA).

Hypoglycemics, Insulin and Related Agents

ADA Standards of Care in Diabetes, 2023

- Recommends initiation of pharmacologic therapy, along with lifestyle changes, at the time of diagnosis for children with T2DM
- Metformin is recommended first-line for asymptomatic children with an HbA1c < 8.5%, while those with marked hyperglycemia and an HbA1c ≥ 8.5% should be initiated on metformin along with long-acting insulin
- If HbA1c goals are not met with metformin (alone or combined with long-acting insulin), the addition of a GLP-1RA approved for youth with T2DM should be considered in patients ≥ 10 years of age
- Patients who do not meet glycemic targets despite treatment with metformin, a GLP-1RA, and long-acting insulin should then be initiated on multiple daily insulin injections or an insulin pump
- The current ADA guidelines do not discuss the use of SGLT2 inhibitors in children with T2DM

Hypoglycemics, Insulin and Related Agents

The Endocrine Society (ES), 2022

- For adults and pediatric patients who are at risk of hypoglycemia, they suggest:
  - The use of long-acting insulin analogs rather than insulin NPH
  - The use of rapid-acting insulin analogs rather than regular (short-acting) human insulins

Hypoglycemics, Insulin and Related Agents

The ADA and EASD, 2022

- Released a consensus report on the management of T1DM in adults.
- The panel emphasizes the importance of an accurate diabetes diagnosis.
- Misclassification of T1DM in adults is common
- Over 40% of those diagnosed with T1DM after the age of 30 years were initially thought to have T2DM.
- They recommend insulin therapy in patients with suspected T1DM, regardless of presence of T2DM features or absence of islet antibodies.
- If the clinical course suggests T2DM, then non-insulin treatment may be tried.

Hypoglycemics, Insulin and Related Agents

American Association of Clinical Endocrinologists (AACE), 2023

- The 2023 algorithm update separates its recommendations into a complications-centric algorithm and a glucose-centric algorithm
- Emphasize a comprehensive approach including individualized targets for weight loss, glucose, lipid, and hypertension management
- AACE supports an HbA1c target of ≤ 6.5% for most patients if it can be reached without substantial hypoglycemia or other adverse effects
- In the complications-centric algorithm, therapy choice is guided by comorbidity rather than by glycemic target
- As such, the algorithm suggests 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 HF should be prescribed an SGLT2 inhibitor, patients with history of stroke or TIA should be initiated on a GLP-1RA or pioglitazone, and patients with CKD should be prescribed an SGLT2 inhibitor or GLP-1RA
- In all cases, a drug with proven CV benefit is recommended
- For these patients, metformin can also be initiated or continued to achieve glycemic targets
- In the glucose-centric algorithm, patients who require glycemic control should begin with lifestyle therapy plus metformin (if appropriate)
- Additional therapies may be added to achieve HbA1c target based on individual patient factors
- For those who are overweight, obese, or at risk for hypoglycemia, a GLP-1RA, dual GLP-1/GIP receptor agonist, or SGLT2 inhibitor is preferred
- For patients with cost or access issues, a TZD, sulfonylurea, or glinide is preferred
- For patients with severe hyperglycemia, basal insulin is preferred in combination with either prandial insulin or a GLP-1RA or dual GLP-1/GIP receptor agonist

Hypoglycemics, Insulin and Related Agents

Product/Guideline Updates:

- American Diabetes Association (ADA) released Standards of Care in Diabetes-2024.
- Key updates regarding medications include:
  - (1) Addition of teplizumab in the Prevention or Delay of Diabetes and Associated Comorbidities section (section 3), which was approved to delay the onset of stage 3 T1DM in adults and peds (aged ≥ 8 yo) with stage 2 T1DM
  - (2) Recommendation added to Obesity and Weight Management for the Prevention and Treatment of Type 2 Diabetes section (section 8) to include GLP-1RAs or a dual GIP/GLP-1 RA with greater weight loss efficacy as preferred pharmacotherapy for obesity management in people with diabetes
  - (3) A recommendation was added to Pharmacologic Approaches to Glycemic Treatment (section 9) stating that pharmacologic therapies should address both individualized glycemic and weight goals in adults with T2DM without CV and/or kidney disease
  - (4) Section 9 updated to reflect preference of insulin analogs or inhaled insulin over injectable human insulins to minimize hypoglycemia risk for most adults with T1DM
  - (5) Recommendation was added to section 9 regarding use of GLT2 inhibitors for glycemic management and prevention of HF hospitalizations

Hypoglycemics, Insulin and Related Agents

Product/Guideline Updates:

- FDA approved Merilog/Merilog SoloStar, the first rapid acting insulin biosimilar product.
- Merilog is a biosimilar to reference product insulin aspart (Novolog) & is a rapid acting human insulin analog indicated to improve glycemic control in adults and pediatric patients with DM (same indication as reference drug Novolog).
- Product will be supplied as 100 units/mL (U-100) in a 10 mL multi-dose vial and 3 mL single-patient-use SoloStar prefilled pen; Novolog (U-100) is also available in a 10 mL multi-dose vial as well as 3 mL single-patient-use FlexPen and FlexTouch prefilled pens and a 3 mL single-patient-use PenFill prefilled cartridge for the 3 mL PenFill cartridge device.
- Recommended dosage is individualized & adjusted based on pt's metabolic needs, blood glucose monitoring results & glycemic control goal.
- Administered as a SC injection within 5-10 minutes before a meal; generally used in a regimen with an intermediate- or long-acting insulin (Novolog is administered SC and IV).

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	Topical treatment of mild to moderate atopic dermatitis in adult and pediatric patients ≥ 3 months of age
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
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
roflumilast (Zoryve®)	Arcutis	Treatment of seborrheic dermatitis in adult and pediatric patients ≥ 9 years of age
ruxolitinib (Opzelura™)	Incyte	Topical short-term and non-continuous chronic treatment of mild to moderate atopic dermatitis in non-immunocompromised patients ≥ 12 years of age whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable

Immunomodulators, Atopic Dermatitis

Drug	Manufacturer	Indications
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 who have failed to respond adequately to other topical prescription treatments for atopic dermatitis, or when those treatments are not advisable ▪ 0.03% ointment approved for patients 2 years to 15 years old ▪ 0.03% ointment and 0.1% ointment approved for adults
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
- Often referred to as “eczema,” AD affects about 17.8 million Americans and accounts for 10% to 20% of all visits to the dermatologist
- Although symptoms of AD can develop at any age, it has been estimated that 60% of patients develop symptoms in the first year of life, while 90% develop symptoms before the age of 5.5 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
- In response to the intense itching, patients may scratch or rub the affected area, which leads to further irritation and inflammation
    - As the skin loses moisture from the epidermal layer, it becomes increasingly dry and may begin to crack, weep, crust, and scale
    - This damage to the integrity of the skin renders it less protective and more prone to infection
    - Despite the chronic nature of this dermatologic condition, there may be periods of the disease when the skin improves and periods when the skin worsens
    - Irritants, such as detergents, fumes, tobacco smoke, and alcohol-containing skin products, and allergens like dust mites, pollen, and animal dander can exacerbate AD or cause “flare ups”
- 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 American Academy of Dermatology (AAD) Guidelines, 2023

- For the management of atopic dermatitis in adults with topical therapies, the guidelines strongly recommend moisturizers, topical corticosteroids, topical calcineurin inhibitors, topical phosphodiesterase 4 (PDE-4) inhibitors (e.g., crisaborole [Eucrisa]), and topical JAK inhibitors (e.g., ruxolitinib cream [Opzelura]) for the treatment of AD
- Topical corticosteroids are typically used first line for mild to severe dermatitis, and medium potency agents are strongly recommended as twice weekly maintenance therapy
- 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; however, it may cause more local irritation and is only formulated as an ointment, which may not be preferable to patients
- For mild to moderate disease, crisaborole has a favorable safety profile and may be used as an alternative to topical corticosteroids and calcineurin inhibitors
- Topical ruxolitinib cream has demonstrated significant efficacy for short-term, non-continuous treatment of mild to moderate AD, but carries the black box warnings inherent to the JAK inhibitor class
- The guidelines note that the strong recommendation for JAK inhibitors in AD is based on moderate certainty, short-term efficacy and safety data and may be updated when longer term data are available
- In the AAD guidelines for use of phototherapy and systemic agents in the treatment of AD, phototherapy is recommended as a treatment option after failure of emollients, topical steroids, and topical calcineurin inhibitors
- Systemic immunomodulating agents are indicated for patients whose AD is not adequately controlled by topical regimens and/or phototherapy
- Dupilumab (Dupixent), tralokinumab-ldrm (Adbry), abrocitinib (Cibinqo), and upadacitinib (Rinvoq) were not available at the time of development of these guidelines

Immunomodulators, Atopic Dermatitis

Product/Guideline Updates:

- Zoryve has been approved as a 0.15% cream for the topical treatment of mild to moderate atopic dermatitis in adults & peds ≥ 6 years of age.
- The 0.3% Zoryve cream was previously approved for topical treatment of plaque psoriasis in adults & pediatric patients ≥ 6 years of age.
- For its new indication, the 0.15% cream should be applied once daily to the affected areas.
- The new strength will be available as a 60 gram tube containing 1.5 mg of roflumilast per gram.

Immunomodulators, Atopic Dermatitis

Product/Guideline Updates:

- Dupixent (dupilumab) is now indicated as add-on maintenance treatment of inadequately controlled chronic rhinosinusitis with nasal polyps (CRSwNP) (previously chronic rhinosinusitis with nasal polyposis) to include pediatric patients as young as 12 years.
- This indication was previously approved for adults.
- The recommended dosage for pediatric patients is the same as for adults: 300 mg subcutaneously every other week.

Immunomodulators, Atopic Dermatitis

Product/Guideline Updates:

- FDA approved Dupixent as an add-on maintenance treatment for adults with inadequately controlled COPD & an eosinophilic phenotype.
- Dupixent is not indicated for relief of acute bronchospasm.
- Recommended dosage for this new indication is 300 mg SC every other week.

Immunomodulators, Atopic Dermatitis

Product/Guideline Updates:

- Bausch has made a business decision to discontinue Elidel.
- Generic formulations are available.

Immunomodulators, Asthma

Drug	Manufacturer	Indications
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
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
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) ▪ Treatment of adult and pediatric patients aged ≥ 12 years with hypereosinophilic syndrome (HES) for ≥ 6 months without an identifiable non-hematologic secondary cause
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 ▪ Chronic rhinosinusitis with nasal polyps (CRSwNP) in adult patients 18 years of age and older with inadequate response to nasal corticosteroids, as add-on maintenance treatment ▪ IgE-mediated food allergy in adult and pediatric patients aged 1 year and older for the reduction of allergic reactions (Type I), including anaphylaxis, that may occur with accidental exposure to one or more foods. To be used in conjunction with food allergen avoidance ▪ Chronic spontaneous urticaria (CSU) in adults and adolescents ≥ 12 years of age who remain symptomatic despite H1 antihistamine treatment
		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

Immunomodulators, Asthma

- Annually, there are approximately 1 million emergency department visits in the United States (US) due to asthma
- An estimated 8.9% of adults and 6.7% of children have asthma in the US
- Asthma is typically characterized by chronic airway inflammation and hyperresponsiveness and is diagnosed based on history of respiratory symptoms (e.g., wheeze, shortness of breath, cough) and evidence of variable expiratory airflow limitation
- Type 2 inflammation is present in most individuals with severe asthma and is characterized by the presence of cytokines (e.g., interleukin [IL]-4, IL-5, IL-13) and elevation of eosinophils or fractional concentration of exhaled nitric oxide (FeNO)

Immunomodulators, Asthma

The Global Initiative for Asthma (GINA), 2024

- The global strategy for asthma management and prevention states:
  - Although most patients will be able to achieve good asthma control with standard management strategies, a subset of patients remain uncontrolled even when treatments are optimized
  - For patients with Type 2 inflammation:
    - A trial of non-biologic therapies is recommended as the first step in treatment, with consideration of individual patient phenotypes
    - If non-biologic interventions are not effective, targeted biologic treatment can be an option, if available
      - Appropriate candidates have exacerbations and/or poor symptom control despite use of at least high-dose ICS/LABA therapy and should display allergic or eosinophilic biomarkers or need maintenance oral corticosteroids (OCS)
      - There are no head-to-head trials directly comparing biologic agents for patients with severe asthma who are eligible for more than one product
      - After a biologic agent is started, treatment should be given for 3-4 months in order to assess response
        - If response is good, treatment may be continued
        - If response is bad, treatment should be stopped, with consideration of a change to an alternative biologic agent
        - If response is unclear, a continued trial for an additional 6-12 months may be recommended

Immunomodulators, Asthma

Product/Guideline Updates:

- Fasenra is now approved for the treatment of adults with eosinophilic granulomatosis with polyangiitis (EGPA).
- The recommended dosage for this new indication is 30 mg every 4 weeks.
- This indication was granted Orphan Drug designation by the FDA.

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 US)
- The 2012 American Academy of Neurology (AAN) guidelines, that were retired in 2022, recommend tetrabenazine, amantadine, or riluzole for chorea associated with HD
- Austedo has not been addressed in these clinical practice guidelines; however, an update to the guidelines is in progress
- Austedo and tetrabenazine have both demonstrated superiority over placebo but have not been compared head-to-head in controlled trials

Movement Disorders

- They state that Austedo or Ingrezza is preferred over tetrabenazine due to the data supporting their use
- Patients with mild TD can also be considered for treatment with a VMAT2 inhibitor following an assessment of several factors
- Ingrezza and Austedo 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

Movement Disorders

- The International Parkinson and Movement Disorder Society (MDS) commissioned an evidence-based review on treatments for Huntington's disease, and results were published in early 2022
  - Using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach, the group appraised 22 randomized controlled trials of 17 interventions targeting several predetermined questions
  - High quality data were limited. Relevant to pharmacotherapeutic treatments in this class, the group found that both deutetrabenazine and tetrabenazine are likely efficacious for chorea
  - They also concluded that deutetrabenazine is likely efficacious for motor impairment, while tetrabenazine is unlikely efficacious

Movement Disorders

- MDS evidence-based review continued:
  - Similarly, deutetrabenazine is 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. Notably, both agents are only approved for the treatment of chorea associated with Huntington's disease
  - Regarding safety of interventions, the group categorized deutetrabenazine as unlikely harmful while tetrabenazine was considered likely harmful

Multiple Sclerosis Agents

ARIZONA HEALTH CARE COST CONTAINMENT SYSTEM

Multiple Sclerosis Agents

Multiple sclerosis (MS)

- Complex human autoimmune-type inflammatory disease of the central nervous system (CNS)
- Although the etiology is predominantly unknown, MS is characterized pathologically by demyelination and subsequent axonal degeneration.
- The nerve degeneration associated with MS can result in a wide variety of symptoms, including sensory disturbances (numbness, paresthesia, burning, and pain) in the limbs, optic nerve dysfunction, ataxia, fatigue, and bladder, bowel, and sexual dysfunction.
- Severe cases may result in partial or complete paralysis.
- Cognitive dysfunction occurs in an estimated 40% to 70% of MS patients, but no correlation exists with the degree of physical disability.
- MS can be categorized as either relapsing-remitting MS (observed in 85% of patients) or primary progressive MS (observed in 15% of patients).
- Relapses or “attacks” typically present sub-acutely, with symptoms developing over hours to several days, persisting for several days or weeks, and then gradually dissipating.

Multiple Sclerosis Agents

Multiple sclerosis (MS)

- The clinical course of MS falls into 1 of the following categories, with the potential to progress from less severe to more serious types:
  - Clinically isolated syndromes (CIS): The first episode of neurologic symptoms due to inflammation or demyelination lasting at least 24 hours. Patients with MRI-detected brain lesions consistent with MS are at high risk of developing MS.
  - Relapsing-remitting MS (RRMS): Clearly defined, self-limited attacks of neurologic dysfunction, followed by periods of remission without disease progression. Most patients experience a recovery of function that is often, but not always, complete.
  - Primary progressive MS (PPMS): Nearly continuous worsening of disease not interrupted by distinct relapses; some of these individuals have occasional plateaus and temporary minor improvements.
  - Secondary progressive MS (SPMS): Relapsing-remitting disease course at onset, followed by progression with or without occasional relapses, minor remissions, and plateaus; most patients eventually convert to progressive MS.

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®)	Biogen-Idec	▪ 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®)	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

Product/Guideline Updates:

- The FDA approved Ocrevus Zunovo (ocrelizumab/hyaluronidase-ocsq), a new formulation combination of ocrelizumab and hyaluronidase-ocsq indicated for the treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and secondary progressive disease in adults AND primary progressive MS in adults.
- Ocrevus Zunovo requires administration by a healthcare provider as a subcutaneous injection into the abdomen and has different dosage/administration instructions than IV ocrelizumab.
- It is supplied as 920 mg of ocrelizumab and 23,000 units of hyaluronidase per 23 mL (40 mg and 1,000 units per mL) solution in a SDV.
- The recommended dosage is 23 mL subcutaneous injection in the abdomen over approximately 10 minutes every 6 months.
- Patients are required to be monitored closely during all injections and for a minimum of 1 hour after the initial injection and for a minimum of 15 minutes after subsequent injections.

Multiple Sclerosis Agents

Product/Guideline Updates:

- FDA has released a Drug Safety Communication regarding the addition of a boxed warning to glatiramer acetate products which describes risk of anaphylaxis that can occur at any time while on treatment, including months or years after initiation.
- Anaphylaxis symptoms typically present within 1 hour of injection.
- Patients should be educated on signs & symptoms of anaphylaxis and should be advised to seek immediate medical attention if any symptoms present.

Opioid Dependence Treatments

ARIZONA HEALTH CARE COST CONTAINMENT SYSTEM

Opioid Dependence Treatments

Class Overview: Buprenorphine Products

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

Class Overview: Buprenorphine/Naloxone Combination Products

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

Opioid Dependence Treatments

Class Overview: Nalmefene Products

- nalmafene HCl nasal spray - (Opvee)

Class Overview: Naloxone Products

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

Class Overview: Naltrexone Products

- naltrexone HCl tablets - (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 46.6 million people aged 12 or older in 2022 were considered to have a substance use disorder (SUD)
- This includes 29.5 million people with an alcohol use disorder, 27.2 million people with an illicit drug use disorder, and 6.1 million with an opioid use disorder
- In 2020, the US Preventive Services Task Force (USPSTF) issued a final recommendation statement on screening for unhealthy drug use.
    - For adults, they recommended screening be implemented when services for accurate diagnosis, effective treatment, and appropriate care can be offered or referred (Grade B).
    - For adolescents, the current evidence is insufficient to determine the benefits and harms of screening for unhealthy drug use (Grade I).

Opioid Dependence Treatments

- Buprenorphine is a partial agonist at the mu-opioid receptor and an antagonist at the kappa-opioid receptor
- Naloxone is an antagonist at the mu-opioid receptor
- Buprenorphine/naloxone was co-formulated in order to prevent patients from abusing buprenorphine in combination with other opioids
- Naltrexone is an opioid antagonist with highest affinity for the mu opioid receptor. Naltrexone 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, generic)
- For some patients, treatment may continue indefinitely
- Suboxone, Zubsolv and the generic should be prescribed based 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; however, it is not a substitute for emergency medical care
- 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

- In April 2021, DHHS released new guidelines, the Practice Guidelines for the Administration of Buprenorphine for Treating OUD, 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
- The Society for Adolescent Health and Medicine published guidelines regarding medication for adolescents and young adults with OUD.
- They state that 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.
- No one agent is recommended over another.

Opioid Dependence Treatments

Product/Guideline Updates:

- The FDA has approved the first nalmefene auto-injector, Zurnai (nalmefene) for the emergency treatment of known or suspected opioid overdose in adults and pediatric patients ≥ 12 years of age.
    - It is an opioid antagonist indicated for emergency treatment of known or suspected opioid overdose induced by natural or synthetic opioids, as manifested by respiratory and/or CNS depression.
- Zurnai is intended for immediate administration as emergency therapy in settings where opioids may be present and is not a substitute for emergency medical care.
- It is supplied as 1.5 mg of nalmefene base/0.5 mL in a prefilled, single-dose autoinjector and can be given IM or SC administered to the outer thigh, through clothing, if needed.
- Additional doses should be administered using a new auto-injector for each dose.
- If the patient does not respond or relapses into respiratory depression following a response, additional doses can be given every 2 to 5 min until emergency medical assistance arrives.

Opioid Dependence Treatments

Product/Guideline Updates:

- FDA approved the first generic to USWM's Lucemyra 0.18 mg tablets from Indoco.

Pancreatic Enzyme

ARIZONA HEALTH CARE COST CONTAINMENT SYSTEM

Pancreatic Enzymes

Class Overview: Products

- Creon
- Pancreaze
- Pertzye
- Viokace
- Zenpep

Pancreatic Enzymes

Class Overview: Product Indications

- 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

Pancreatic Enzymes

Class Overview: Product Indications

- 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

Class Summary:

- Pancreatic enzyme supplements differ in enzyme content and bioavailability
- These products have demonstrated favorable risk-benefit profiles in the treatment of exocrine pancreatic insufficiency due to cystic fibrosis and other conditions
- Dosing of these products should be individualized in accordance with the individual product's prescribing information and the CFF Consensus Guidelines

Stimulants and Related Agents

ARIZONA HEALTH CARE COST CONTAINMENT SYSTEM

Stimulants and Related Agents

Class Overview: Product Indications

- ADHD (attention deficit hyperactivity disorder), Narcolepsy
- Other: exogenous obesity, binge eating disorder

Stimulants and Related Agents

Drug	Manufacturer	ADHD			Narcolepsy (Age ≥6 years)	Other Indications
		Age 3–5 years	Age ≥ 6 years	Adults		
Stimulants: Immediate-Release						
amphetamine sulfate (Evekeo™)	generic, Arbor	X	X	--	X	Exogenous obesity age ≥12 years
amphetamine sulfate orally disintegrating tablet (ODT) (Evekeo ODT™)	Arbor	--	X			
dexmethylphenidate IR (Focalin ®)	generic, Novartis	--	X	--	--	--
dextroamphetamine IR	generic	X	X (≤ 16 years)	--	X	--
dextroamphetamine solution	generic	X	X (≤ 16 years)	--	X	--

Stimulants and Related Agents

Drug	Manufacturer	ADHD			Narcolepsy (Age ≥6 years)	Other Indications
		Age 3–5 years	Age ≥ 6 years	Adults		
Stimulants: Immediate-Release						
methamphetamine (Desoxyn®)	generic, Recordati	--	X	--	--	Exogenous obesity in adults and adolescents ≥ 12 years of age
methylphenidate IR (Methylin, Ritalin®)	generic, Shionogi	--	X	--	X	--
mixed amphetamine salts IR (Adderall®)	generic, Teva	X	X	--	X	--
modafinil (Provigil®)	generic, Cephalon/Teva	--	--	--	--	Excessive sleepiness associated with narcolepsy, OSA†, and SWD for age ≥ 17 years

Stimulants and Related Agents

Drug	Manufacturer	ADHD			Narcolepsy (Age ≥6 years)	Other Indications
		Age 3–5 years	Age ≥ 6 years	Adults		
Stimulants: Extended-Release						
amphetamine ER (Adzenys ER, XR-ODT™)	generic,Neos	--	X	X	--	--
amphetamine ER (Dyanavel® XR)	Tris	--	X	X	--	--
dexmethylphenidate ER (Focalin XR®)	generic, Novartis	--	X	X	--	--
dextroamphetamine ER (Dexedrine®)	generic., Amedra	--	X (≤ 16 years)	--	X	--
dextroamphetamine transdermal (Xelstrym™)	Noven	--	X	X	--	--
lisdexamfetamine dimesylate (Vyvanse®)	Shire	--	X	X	--	Moderate to severe binge eating disorder in adults

Stimulants and Related Agents

Drug	Manufacturer	ADHD			Narcolepsy (Age ≥6 years)	Other Indications
		Age 3–5 years	Age ≥ 6 years	Adults		
Stimulants: Extended-Release						
methylphenidate ER	generic	--	X	--	--	--
methylphenidate ER (Adhansia XR™)	Adlon	--	X	X	--	--
methylphenidate ER (Aptensio XR®)	generic, Rhodes	--	X	X	--	--
methylphenidate ER (Cotempla XR-ODT®)	Neos	--	X	--	--	--
methylphenidate ER (Jornay PM™)	Ironshore	--	X	X	--	--
methylphenidate ER (Metadate ER®, Ritalin SR®	generic, Upstate	--	X	X	X	--
methylphenidate ER (QuilliChew™ ER)	Tris	--	X	X	--	--
methylphenidate ER (Quillivant XR®)	Tris	--	X	X	--	

Stimulants and Related Agents

Drug	Manufacturer	ADHD			Narcolepsy (Age ≥6 years)	Other Indications
		Age 3–5 years	Age ≥ 6 years	Adults		
Stimulants: Extended-Release						
methylphenidate ER (Ritalin LA®)	generic, Novartis	--	X	--	--	--
methylphenidate ER OROS (Concerta®)	generic, Janssen	--	X	X	--	--
methylphenidate ER OROS (Relexxii®)	Vertical	--	X	X (≤ 65 years)	--	--
methylphenidate transdermal (Daytrana®)	Noven	--	X	--	--	--
mixed amphetamine salts ER (Adderall XR®)	generic, Shire	--	X	X	--	--
mixed amphetamine salts ER (Mydayis®)	Shire	--	--	-- (≥ 13 years)	--	--
serdexmethylphenidate/ dexmethylphenidate (Azstarys®)	Corium/Prasco	--	X	X	--	--

Stimulants and Related Agents

Drug	Manufacturer	ADHD			Narcolepsy (Age ≥6 years)	Other Indications
		Age 3–5 years	Age ≥ 6 years	Adults		
Non-Stimulants						
atomoxetine (Strattera®)	generic, Eli Lilly	--	X	X	--	--
clonidine ER (Kapvay®)	Generic, Concordia	--	X	--	--	Treatment of ADHD as adjunct to stimulants
guanfacine ER (Intuniv®)	generic, Shire	--	X	--	--	Treatment of ADHD as adjunct to stimulants
pitolisant (Wakix®)	Harmony	--	--	--	X (adults only)	--
solriamfetol (Sunosi®)	Jazz/Axsome	--	--	--	X (adults only)	OSA (adults)**
viloxazine (Qelbree®)	Supernus	--	X	X	--	--

Stimulants and Related Agents

Attention Deficit Hyperactivity Disorder (ADHD)

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

The Medical Letter, 2020

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

Stimulants and Related Agents

Class Summary:

- The AAP guidelines now also include a recommendation to screen patients for comorbidities such as depression, anxiety and substance use.
- The individual agents used for the treatment of ADHD are associated with different contraindications and precautions for use
- This may influence the selection of appropriate therapy in patients with comorbidities (e.g., coexistent tic disorders or Tourette's syndrome)
- The 2019 AAP Clinical Practice Guideline for children with ADHD recommends stimulant medication and/or behavioral therapy for the treatment of ADHD in children

Stimulants and Related Agents

Class Summary:

- The guideline states that, in many cases, the stimulants improve the child's ability to follow rules and decrease emotional overactivity, leading to improved relationships and performance
- Studies have shown that 70% to 75% of patients respond to the first stimulant medication on which they are started; response increases to 90% to 95% when a second stimulant is tried
- Once-daily dosage forms may enhance compliance and decrease the risk of diversion

Stimulants and Related Agents

Class Summary:

- Vyvanse is the first and only FDA-approved treatment for moderate to severe binge eating disorder in adults
- Jornay PM is dosed in the evening prior to its expected effect, as the pharmacokinetics of the formulation result in drug exposure beginning the following morning
- Except for atomoxetine (Strattera), clonidine ER (Kapvay), guanfacine ER (Intuniv), and viloxazine (Qelbree), all of the drugs approved for treatment of ADHD by the FDA are stimulants and are classified as controlled substances

Stimulants and Related Agents

Product/Guidelines Updates:

- FDA has approved clonidine ER oral suspension (Onyda XR) for treatment of ADHD as monotherapy or as adjunctive treatment to CNS stimulant medications in pediatric patients ≥ 6 years of age.
- Recommended starting dosage is 0.1 mg orally once daily at bedtime; dose may then be increased by 0.1 mg/day increments at weekly intervals according to pt response, up to a max dose of 0.4 mg daily.
- Onyda XR may not be substituted for other clonidine products on a mg-per-mg basis due to differing PK profiles.
- Dose must be tapered down upon discontinuation to avoid rebound hypertension.
- Product will be available as 0.1 mg/mL ER oral suspension.

Stimulants and Related Agents

Product/Guidelines Updates:

- FDA announced that Eli Lilly made a business decision to discontinue marketing Stattera (10 mg, 18 mg, 25 mg, 40 mg, 60 mg, 80 mg and 100 mg).
- Generics remain available.
- Strattera is an SNRI indicated for the treatment of ADHD.

New Drug Reviews

ARIZONA HEALTH CARE COST CONTAINMENT SYSTEM

New Drugs

1. Alyftrek - vanzacaftor, tezacaftor, and deutivacaftor
2. Crenessity - crinecerfont
3. Kebilidi - eladocagene exuparvovec-tneq
4. Tryngolza - olezarsen
5. Tryvio - aprocitentan

Alyftrek (vanzacaftor/tezacaftor/deutivacaftor)

- Approved for the treatment of cystic fibrosis in patients ≥ 6 years of age who have ≥ 1 F508del mutation or another responsive mutation in the CFTR gene.
- If a patient's genotype is unknown, an FDA-cleared CF mutation test should be used to confirm presence of an indicated mutation.
- Dosing:
    - For patients 6 to < 12 years of age who weigh < 40 kg, dosage is 3 tablets of vanzacaftor 4 mg/tezacaftor 20 mg/deutivacaftor 50 mg orally once daily.
    - For patients 6 to < 12 years of age who weigh ≥ 40 kg and for patients ≥ 12 years of age, dosage is 2 tablets of vanzacaftor 10 mg/tezacaftor 50 mg/deutivacaftor 125 mg orally once daily.
- Available as tablets containing a fixed-dose combo of vanzacaftor 4 mg, tezacaftor 20 mg, & deutivacaftor 50 mg and vanzacaftor 10 mg, tezacaftor 50 mg, & deutivacaftor 125 mg.
- Alyftrek carries a boxed warning for drug-induced liver injury & liver failure.
- The most common adverse reactions were cough, nasopharyngitis, upper respiratory tract infection, headache, oropharyngeal pain, influenza, fatigue, increased ALT and AST, rash, and sinus congestion.

Alyftrek (vanzacaftor/tezacaftor/deutivacaftor)

NCT05033080 and NCT05076149

- The efficacy of Alyftrek in patients aged 12 years and older with cystic fibrosis (CF) who have at least one F508del mutation or a responsive mutation in the CFTR gene was evaluated in two 52-week randomized, double-blind, active-controlled trials comparing Alyftrek and a fixed-dose combination drug containing elexacaftor, tezacaftor, and ivacaftor (ELX/TEZ/IVA).
- The two trials enrolled a total of 971 patients aged 12 years and older with CF who have at least one F508del mutation or other ELX/TEZ/IVA-responsive mutations in the CFTR gene.
    - Because patients in Trial 1 and Trial 2 would receive ELX/TEZ/IVA, patients with a history of intolerance to ELX/TEZ/IVA were excluded from these trials.
- Trial 1 enrolled patients with CF heterozygous for F508del and a CFTR mutation that results in a protein that was not responsive to ivacaftor or tezacaftor/ivacaftor (minimal function mutation). A total of 398 patients with CF aged 12 years and older received a daily oral dosage of ELX/TEZ/IVA (elexacaftor 200 mg/tezacaftor 100 mg/ivacaftor 150 mg in the morning and ivacaftor 150 mg in the evening) during a 4-week run-in period and were then randomized to receive ALYFTREK (total once daily oral dosage of vanzacaftor 20 mg/tezacaftor 100 mg/deutivacaftor 250 mg) or ELX/TEZ/IVA (same dosage as in the run-in period) during the 52-week treatment period.

Alyftrek (vanzacaftor/tezacaftor/deutivacaftor)

NCT05033080 and NCT05076149 (Continued)

- Trial 2 enrolled patients with CF who had one of the following genotypes: homozygous for the F508del mutation, heterozygous for the F508del mutation and either a gating or a residual function mutation, at least one mutation responsive to ELX/TEZ/IVA with no F508del mutation. A total of 573 patients with CF aged 12 years and older received a daily oral dosage of ELX/TEZ/IVA (elexacaftor 200 mg/tezacaftor 100 mg/ivacaftor 150 mg in the morning and ivacaftor 150 mg in the evening) during a 4-week run-in period and were then randomized to receive ALYFTREK (total once daily oral dosage of vanzacaftor 20 mg/tezacaftor 100 mg/ deutivacaftor 250 mg) or ELX/TEZ/IVA (same dosage as during the run-in period) during the 52-week treatment period.
- In both trials, the primary endpoint evaluated non-inferiority in mean absolute change in ppFEV1 from baseline through Week 24 and a key secondary endpoint evaluated the mean absolute change from baseline in sweat chloride through Week 24 in the Alyftrek and ELX/TEZ/IVA treatment groups.

Alyftrek (vanzacaftor/tezacaftor/deutivacaftor)

NCT05033080 and NCT05076149 (Continued)

- In Trial 1, treatment with Alyftrek resulted in an LS mean difference of 0.2 percentage points (95% CI: -0.7, 1.1) in absolute change in ppFEV1 from baseline through Week 24 compared to ELX/TEZ/IVA.
- In Trial 2, treatment with Alyftrek resulted in an LS mean difference of 0.2 percentage points (95% CI: -0.5, 0.9) in absolute change in ppFEV1 from baseline through Week 24 compared to ELX/TEZ/IVA.

Crenessity (crinecerfont)

- The FDA has approved crinecerfont (Crenessity), a corticotropin-releasing factor type 1 receptor antagonist, indicated as adjunctive treatment to glucocorticoid (GC) replacement to control androgens in adults and peds pts ≥ 4 years of age with classic congenital adrenal hyperplasia (CAH).
- Supplied as an oral solution in the strength of 50 mg/mL and oral capsules in the strengths of 25 mg, 50 mg and 100 mg.
- GC replacement therapy for adrenal insufficiency associated with CAH should be continued with crinecerfont; androstenedione levels can be assessed starting 4 weeks after initiation of this medication to determine if a decrease in GC dose is indicated (do not decrease the GC dose below that needed for replacement tx).
- Recommended dosage for adults is 100 mg orally, twice daily with a meal in the morning and evening.
- Recommended dosage for peds pts is weight-based, taken orally, twice daily with a meal in the morning and evening.

Crenessity (crinecerfont)

NCT04490915

- The efficacy of Crenessity to reduce androgen levels and enable a reduced glucocorticoid dose while maintaining androgen control in adults with classic CAH was evaluated in a randomized, double-blind, placebocontrolled study
- This study enrolled 182 adults with classic CAH due to 21-hydroxylase deficiency on supraphysiological glucocorticoid doses and with androgen concentrations in the normal range or with inadequate androgen control.
- Subjects were randomized to receive Crenessity 100 mg twice daily (N=122) or placebo (N=60) for 24 weeks.
    - During the first 4 weeks of Crenessity treatment, subjects maintained a stable glucocorticoid regimen except for stress dosing as needed.
    - During Weeks 4 to 12, the glucocorticoid dose was reduced as frequently as every 2 weeks without regard to androstenedione levels, with the goal to achieve a glucocorticoid dose of 8 to 10 mg/m2 /day in hydrocortisone dose equivalents adjusted for body surface area by Week 12.
    - From Weeks 12 to 20, the glucocorticoid dose was further adjusted, if needed, to achieve androstenedione control by Week 24.

Crenessity (crinecerfont)

NCT04490915 (Continued)

- The efficacy of Crenessity was assessed by the least-squares (LS) mean (SEM) percent change from baseline in the total glucocorticoid daily dose while androstenedione was controlled (≤120% of baseline or ≤upper limit of normal [ULN]) after 24 weeks.
- The LS mean percent change from baseline in daily glucocorticoid dose was statistically significantly greater in the Crenessity group at -27% compared to -10% in the placebo group.
- At Week 24, there was a statistically significantly greater percentage of subjects achieving a reduction to a physiologic glucocorticoid daily dose (≤11 mg/m2 /day hydrocortisone equivalents) while androstenedione was controlled (≤120% of baseline or ≤ULN) with Crenessity compared to placebo (63% vs 18%, p<0.0001).

Kebilidi (eladocagene exuparvovec-tneq)

- The FDA has granted Accelerated Approval to eladocagene exuparvovec-tneq (Kebilidi), an adeno-associated virus (AAV) vector-based gene therapy indicated for the treatment of adult and pediatric pts with aromatic L-amino acid decarboxylase (AADC) deficiency.
  - The Accelerated Approval is based on change from baseline in gross motor milestones at 48 weeks post-treatment; continued approval for this use may require demonstration of benefit in a confirmatory clinical trial.
  - Patients should be confirmed to have AADC deficiency due to biallelic mutations in the DDC gene.
- Supplied as a suspension with a nominal concentration of 5.6 x1011 vg/mL in an SDV that contains 2.8 x1011 vg in an extractable volume of 0.5 mL.
- Administered via intraputaminal infusion only.
- The recommended dosage is 1.8 x1011 vg (0.32 mL total volume).
  - The dose is delivered as four 0.08 mL (0.45 x1011 vg) infusions (two sites per putamen-anterior and posterior) at a rate of 0.003 mL/minutes for a total of 27 minutes per site during a single stereotactic surgery (cannula that is used should be FDA-authorized for intraparenchymal infusion).
- Brain imaging should be performed before the procedure for stereotactic planning and intraoperative navigation; surgical access through the skull bone and dura should be performed for administration.
- The gene therapy should be administered in a medical center specializing in stereotactic neurosurgery.

Kebilidi (eladocagene exuparvovec-tneq)

NCT04903288

- The efficacy of Kebilidi was evaluated in one open-label, single arm study.
- The study enrolled pediatric patients with genetically confirmed, severe AADC deficiency who had achieved skull maturity assessed with neuroimaging.
- The main efficacy outcome measure was gross motor milestone achievement evaluated at week 48 and assessed using the Peabody Developmental Motor Scale, Second Edition (PDMS-2).
- Patients treated with Kebilidi were compared to an external untreated natural history cohort of 43 pediatric patients with severe AADC deficiency who had at least one motor milestone assessment after 2 years of age.
- A total of 13 patients received a single total dose of $1.8X10^{11}$ vg of Kebilidi given as four intraputaminal infusions in a single stereotactic neurosurgical procedure.
- Twelve of the 13 patients had the severe phenotype of AADC deficiency, defined as having no motor milestone achievement at baseline and no clinical response to standard of care therapies.
- The one remaining patient had a “variant” of the severe disease phenotype, with the ability to sit with assistance but with lack of head control.
- Gross motor milestone achievement at Week 48 was assessed in 12 of the 13 patients treated in Study 1 (one patient dropped out of the study prior to Week 48)

Kebilidi (eladocagene exuparvovec-tneq)

NCT04903288 (Continued)

- Eight (67%) of the 12 treated patients achieved a new gross motor milestone at week 48:
  - 3 patients achieved full head control
  - 2 patients achieved sitting with or without assistance
  - 2 patients achieved walking backwards and the patient with the “variant” severe phenotype was able to sit unassisted.
  - The two patients who achieved walking backwards at week 48 were treated before 2 years of age.
  - The four patients who were unable to achieve new gross motor milestones at week 48 were treated between the ages of 2.8 and 10.8 years.
- In comparison, none of the 43 untreated patients with the severe phenotype had documented motor milestone achievement at last assessment at a median age of 7.2 years (range 2 to 19 years).

Tryngolza (olezarsen)

- The FDA approved olezarsen (Tryngolza), an apolipoprotein C-III (APOC-III)-directed antisense oligonucleotide (ASO) indicated as an adjunct to diet to reduce triglycerides in adults with familial chylomicronemia syndrome (FCS).
- This first-in-class agent will be supplied as 80 mg/0.8 mL in a single-dose autoinjector.
- Recommended dosage is 80 mg SC once monthly administered into the abdomen or front of the thigh; back of upper arm can also be an injection site if given by caregiver or Healthcare Practitioner.
- Most common adverse reactions were injection site reactions, decreased platelet count, and arthralgia.

Tryngolza (olezarsen)

NCT04568434

- The efficacy of Tryngolza was demonstrated in a randomized, placebo-controlled, double-blind clinical trial in adult patients with genetically identified FCS and fasting triglyceride (TG) levels ≥880 mg/dL.
- After a ≥4-week run-in period where patients continued to follow a low-fat diet with ≤20 grams fat per day, patients were randomly assigned to receive doses every 4 weeks of Tryngolza 80 mg (n=22) or matching volume of placebo (n=23) via subcutaneous injection over a 53-week treatment period.
- The proportion of patients with diabetes at enrollment was 32% in the Tryngolza 80 mg group compared with 26% in the placebo group.
- Patients in the Tryngolza 80 mg and placebo groups were treated with statins (27%), omega-3 fatty acids (42%), fibrates (49%), or other lipid lowering therapies (13%) at study entry.
- Seventy-one percent (71%) of patients in the Tryngolza 80 mg and placebo groups combined had a history of documented acute pancreatitis in the prior 10 years.
- The primary endpoint was percent change in fasting triglycerides from baseline to Month 6 (average of Weeks 23, 25, and 27) compared to placebo.
- The difference between Tryngolza 80 mg group and the placebo group in percent change in fasting triglycerides from baseline to Month 6 was -42.5% (95% CI: -74.1%, -10.9%; p=0.0084).

Tryvio (aprocitentan)

- The FDA has approved aprocitentan (Tryvio), an endothelin receptor antagonist, indicated for the treatment of hypertension in combo with other antihypertensive drugs, to lower blood pressure in adults who are not adequately controlled on other drugs.
- Supplied as an oral tablet in the strength of 12.5 mg.
- Recommended dosage of 12.5 mg orally once daily with or without food.
- Boxed warning for embryo-fetal toxicity.
- Most common adverse reactions are edema/fluid retention and anemia.

Tryvio (aprocitentan)

NCT03541174

- The efficacy of Tryvio (aprocitentan) was evaluated in a multipart, phase 3 multicenter study in adults with SBP ≥140 mmHg who were prescribed at least three antihypertensive medications.
- The trial included a placebo run-in period, which was followed by three parts as described below.
- Prior to the placebo run-in period, all patients were switched to standard background antihypertensive therapy consisting of an angiotensin receptor blocker, a calcium channel blocker, and a diuretic, which was continued throughout the study.
- Patients with concomitant use of beta-blockers continued this treatment throughout the study.
- Following the 4-week placebo run-in period, 730 patients were randomized equally to aprocitentan at either 12.5 mg, 25 mg, or placebo once daily during the initial 4-week double-blind (DB) treatment period (part 1).
- At the end of 4 weeks, all patients entered the single-blind treatment period (part 2) where they received 25 mg aprocitentan once daily for 32 weeks.
- At the end of the 32 weeks, patients were re-randomized to receive either 25 mg aprocitentan or placebo, once daily, during a 12-week DB-withdrawal period.

Tryvio (aprocitentan)

NCT03541174 (Continued)

- The primary efficacy endpoint was the change in sitting SBP (SiSBP) from baseline to Week 4 during part 1, measured at trough by unattended automated office blood pressure (uAOBP).
- The key secondary endpoint was the change in SiSBP measured at trough by uAOBP from Week 36 (i.e., prior to randomized withdrawal to 25 mg aprocitentan or placebo in part 3) to Week 40.
- BP reductions for treatment compared to placebo based on uAOBP measurements were found to be statistically significant (p= 0.0043).
- In part 3 of the trial, patients on aprocitentan were re-randomized to placebo or 25 mg aprocitentan following a period during which all patients were treated with 25 mg.
- In patients re-randomized to placebo, the mean SiSBP increased, whereas in patients re-randomized to 25 mg aprocitentan the mean effect on SiSBP was maintained and was statistically superior to placebo at Week 40.

Break and Executive Session

ARIZONA
HEALTH CARE COST
CONTAINMENT SYSTEM

Public Therapeutic Class Votes

ARIZONA HEALTH CARE COST CONTAINMENT SYSTEM

Biosimilar Update

ARIZONA HEALTH CARE COST CONTAINMENT SYSTEM

Biosimilar Update
Effective Date for Changes: August 1, 2025

Brand Name Product	Generic Name	Preferred Biosimilar Label Name	Preferred Biosimilar Chemical Name	Preferred Products Moving to Non-Preferred Status	Preferred Biosimilar Manufacturer
Eylea	Aflibercept	***Pavblu***	***Aflibercept-ayyh***	New Addition	Amgen
Humira	Adalimumab	Unbranded Version Hadlima	***Adalimumab-fjkp*** ***Adalimumab- bwwd***	Simlandi Adalimumab-abdm	Biocon Biologics Organon
Avastin	Bevacizumab	***MVASI*** ***Zirabev***	***Bevacizumab-awwb*** ***Bevacizumab-bvzr***	No Changes	Amgen Pfizer
Soliris	Eculizumab	***Epysqli***	***Eculizumab-aagh***	New Addition	Teva
Neupogen	Filgrastim	Releuko Nivestym	Filgrastim-ayow Filgrastim-aafi	Neupogen	Amneal Pfizer
Neulasta	Pegfilgrastim	Fulphila Fylnetra	Pegfilgrastim-jmdb Pegfilgrastim-pbbk	Undenyca Nyvepria Ziextenzo	Mylan Amneal
Lucentis	Ranibizumab	***Cimerli***	***Ranibizumab-eqrn***	New Addition	Sandoz
Rituxan	Rituximab	***Riabni*** Ruxience	***Rituximab-arrx*** ***Rituximab-pvvr***	Truxima	Amgen Pfizer
Actemra	Tocilizumab	***Tyenne***	***Tocilizumab-aazg***	New Addition	Fresenius
Herceptin	Trastuzumab	***Ogivri***	***Trastuzumab-dkst***	Kanjinti, Herzuma Trazimera	Mylan-Biocon Biologics
Stelara	Ustekinumab	***Yesintek***	***Ustekinumab-kfce***	New Addition	Biocon Biologics

AHCCCS P&T Committee Future Meeting Dates:

October 22, 2025
January 13, 2026
May 19, 2026
October 21, 2026
January 26, 2027

ARIZONA HEALTH CARE COST CONTAINMENT SYSTEM