ARIZONA
HEALTH CARE COST
CONTAINMENT SYSTEM

AHCCCS Pharmacy and Therapeutics Committee

January 15th, 2025

P&T Agenda

- Welcome and Introductions
- Supplemental Rebate Class Reviews
- New Drug Reviews
- Executive Session
- Public Therapeutic Class Votes
- Meeting Adjournment

Welcome and Introductions

- Suzi Berman, RPh, Pharmacy Director, AHCCCS
  - ❑ Minutes Review and Vote - P&T October 16th, 2024
  - ❑ Review
  - ❑ Vote

Prime Therapeutics Class Reviews

Classes for Review: Non-Supplemental Rebate Classes

- Adrogenic Agents
- Antidepressants, Other
- Antidepressants, SSRIs
- Antivirals, Topical
- Bone Resorption Suppression and Related Agents
- Bronchodilators, Beta Agonists
- Enzyme Replacement, Gaucher Disease
- Erythropoiesis Stimulating Proteins
- Hypoglycemics, Alpha Glucosidase Inhibitors
- Hypoglycemics, Metformins
- Hypoglycemics, SGLT2s
- Immune Globulins
- Oncology, Oral - Hematologic
- Ophthalmics, Anti-inflammatory/ Immunomodulators
- Otic Antibiotics
- Pulmonary Arterial Hypertension Agents
- Thrombopoiesis Stimulating Agents
- Ulcerative Colitis

Prime Therapeutics Drug Class Reviews

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Androgenic Agents

Androgenic Agents

Drug	Manufacturer	Indications
testosterone gel (Androgel®)[1,2]	generic, Abbvie, Ascend	Testosterone replacement therapy in males for conditions associated with a deficiency or absence of endogenous testosterone, such as primary or secondary hypogonadism (congenital or acquired)*
testosterone gel (Fortesta®)[3]	generic, Endo	
testosterone gel (Testim®)[4]	Auxilium/Endo	
testosterone gel (Vogelxo®)[5]	generic, Upsher-Smith	
testosterone nasal gel (Natesto®)[6]	Aytu Biopharma, Acerus	
testosterone solution†[7]	generic	
testosterone transdermal system (Androderm®)[8]	Allergan	

Androgenic Agents

Male Hypogonadism

- Male hypogonadism is caused by insufficient production of testosterone and is characterized by low serum concentrations. Hypogonadism may present as testosterone deficiency, infertility, or both
- Symptoms at presentation will primarily depend on the patient's age at the time of disease onset and can include impotence, decreased libido, fatigue, loss of energy, mood, depression, and regression of secondary sex characteristics
- Potential risks due to male hypogonadism include osteoporosis, sexual dysfunction, depression, and cardiovascular disease
- After 30 years of age, testosterone levels in men decrease at rates up to 2% annually
- Causes of hypogonadism are classified as primary, due to failure of the testes, or secondary, due to failure of the hypothalamus or pituitary gland
- Either type of hypogonadism may be caused by an inherited (congenital) or acquired factor
- Conditions resulting in primary hypogonadism include cryptorchidism, bilateral torsion, orchitis, vanishing testis syndrome, orchidectomy, chemotherapy, radiation therapy, toxic damage from alcohol or heavy metals, testicular infections (such as mumps) and chromosomal abnormalities such as Klinefelter's Syndrome
- Patients usually present with low testosterone levels and elevated follicle stimulating hormone (FSH) and luteinizing hormone (LH) levels
- Secondary (hypogonadotropic) hypogonadism includes idiopathic gonadotropin or luteinizing hormone releasing hormone (LHRH) deficiency and pituitary hypothalamic injury from tumors, trauma, or radiation
- Testosterone levels are low in patients with secondary hypogonadism, and FSH and LH levels are low or in the normal range

Androgenic Agents

American College of Physicians, 2020

- A clinical guideline on testosterone treatment for adult men with age-related low testosterone
- This guideline has been endorsed by the American Academy of Family Physicians (AAFP) and suggests a discussion between clinicians and patients regarding if testosterone therapy should be started for men with age-related low T with sexual dysfunction who want to improve sexual function; patient's preferences as well as benefits and risks of therapy should be considered
- It is suggested that symptoms be reassessed within 12 months and periodically, and testosterone therapy be discontinued in patients with no improvement in sexual function.
- Although clinical efficacy and safety are comparable for transdermal and intramuscular (IM) testosterone treatment, costs are lower for IM formulations.
- These formulations are suggested for improving sexual function when starting testosterone therapy
- It is suggested not to start testosterone therapy for improvement of energy, vitality, physical function, or cognition in men with age-related low T

Androgenic Agents

American Urological Association (AUA), 2018

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

Androgenic Agents

- In May 2009, FDA issued a safety alert for testosterone gel products due to reports of children experiencing adverse effects after unintended exposure to testosterone through contact with individuals being treated with these agents
- As a result, all gel and solution products carry a boxed warning on virilization of children following secondary exposure
- The FDA issued a warning that prescription testosterone products are approved only for men who have low testosterone levels caused by certain medical conditions

Androgenic Agents

- In 2015 the FDA stated that there is a possible increased cardiovascular risk associated with testosterone use
- The TRAVERSE study, which was published in 2023, found that testosterone replacement therapy did not have a higher incidence of major adverse cardiac events compared to placebo in males with hypogonadism and preexisting or high risk of CVD
- The gel and solution formulations of testosterone have demonstrated a lower incidence of adverse reactions related to administration compared to the patches
- All testosterone products are Schedule III controlled substances

Antidepressants, Other

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Antidepressants, Other

Drug	Manufacturer	Major Depressive Disorder (MDD)	Generalized Anxiety Disorder (GAD)	Social Anxiety Disorder (SAD)	Panic Disorder	Other Indications
bupropion HBr ER (Aplenzin)	Bausch	X	--	--	--	prevention of seasonal major depressive episodes associated with seasonal affective disorder
bupropion HCl ER (Forfivo XL)	generic, Almatica	X	--	--	--	--
bupropion HCl ER (Wellbutrin XL)	generic, Bausch	X	--	--	--	prevention of seasonal major depressive episodes associated with seasonal affective disorder
bupropion HCl IR	generic	X	--	--	--	--
bupropion HCl SR (Wellbutrin SR)	generic, GlaxoSmithKline	X	--	--	--	--
desvenlafaxine ER base	Ranbaxy/Sun	X	--	--	--	--
desvenlafaxine succinate ER (Pristiq)	generic, Wyeth/Pfizer	X	--	--	--	--
dextromethorphan HBr/bupropion ER (Auvelity)	Axsome	X	-	-	-	-
duloxetine HCl DR (Cymbalta)	generic, Eli Lilly	X	X	--	--	diabetic peripheral neuropathic pain; fibromyalgia; chronic musculoskeletal pain
duloxetine HCl DR* (Drizalma Sprinkle)	Sun	X	X	--	--	diabetic peripheral neuropathic pain; fibromyalgia; chronic musculoskeletal pain

Antidepressants, Other

Drug	Manufacturer	Major Depressive Disorder (MDD)	Generalized Anxiety Disorder (GAD)	Social Anxiety Disorder (SAD)	Panic Disorder	Other Indications
esketamine (Spravato)	Janssen	X treatment-resistant depression (TRD); depressive symptoms with acute suicidal ideation or behavior	--	--	--	--
isocarboxazid (Marplan)	Validus	X 2nd line therapy	--	--	--	--
Levomilnacipran (Fetzima)	Allergan/Forest	X	--	--	--	--
mirtazapine tablet and ODT (Remeron; Remeron SolTab)	generic, Merck, Organon	X	--	--	--	--
nefazodone	Teva	X	--	--	--	--
phenelzine (Nardil)	Greenstone, Pfizer	X 2nd line therapy	--	--	--	--
selegiline (Emsam)	Mylan Specialty	X	--	--	--	--
tranylcypromine (Parnate)	generic, Concordia	X 2nd line therapy	--	--	--	--
trazodone	generic	X	--	--	--	--
esketamine (Spravato)	Janssen	X treatment-resistant depression (TRD); depressive symptoms with acute suicidal ideation or behavior	--	--	--	--

Antidepressants, Other

Drug	Manufacturer	Major Depressive Disorder (MDD)	Generalized Anxiety Disorder (GAD)	Social Anxiety Disorder (SAD)	Panic Disorder	Other Indications
venlafaxine besylate ER (Venlafaxine Besylate ER)	Almatica	X	X	--	--	--
venlafaxine HCl IR	generic	X	--	--	--	--
venlafaxine HCl ER capsule (Effexor XR)	generic, Pfizer/Viatris	X	X	X	X	--
venlafaxine HCl ER tablet (Venlafaxine ER)	generic	X	--	X	--	--
vilazodone HCl (Viibryd)	generic, Allergan	X	--	--	--	--
vortioxetine (Trintellix)	Takeda	X	--	--	--	--
zuranolone (Zurzuvae)	Biogen	--	--	--	--	postpartum depression
venlafaxine besylate ER (Venlafaxine Besylate ER)	Almatica	X	X	--	--	--
venlafaxine HCl IR	generic	X	--	--	--	--
venlafaxine HCl ER capsule (Effexor XR)	generic, Pfizer/Viatris	X	X	X	X	--

Antidepressants, Other

- In 2020 about 8.4% of the adult population in the US, which translates to about 21 million adults have reported experiencing depression
- The prevalence of depression among adolescents (ages 12 to 17 years) in 2020 was estimated to be 4.1 million
- Generalized anxiety disorder (GAD) and social anxiety disorder (SAD) affect about 6.8 million and 15 million adult Americans, respectively
- It is estimated that panic disorder will affect 4.7% of adults in the US during their lifetime

Antidepressants, Other

- ACP published a 2023 guideline on nonpharmacologic and pharmacologic treatments of adults in the acute phase of MDD
- The guideline states that patients with acute mild MDD should initiate CBT as initial treatment
- Patients with acute moderate or severe MDD undergo monotherapy with either CBT or a second-generation antidepressant (e.g., SSRI, SNRI, bupropion, mirtazapine, nefazodone, trazodone, vilazodone, vortioxetine)
- Combination therapy with CBT and a second-generation antidepressant can be considered as initial therapy for certain patients with moderate to severe MDD

Antidepressants, Other

- The American Academy of Child and Adolescent Psychiatry (AACAP) published a 2023 guideline for the assessment and treatment of children and adolescents with MDD
- AACAP suggests the use of an SSRI, particularly fluoxetine and excluding paroxetine, as an option for children and adolescents with MDD
- Combination therapy with CBT and fluoxetine could also be offered to this patient population
- The 2023 WFSBP guidelines recommend SSRIs and SNRIs as first-line therapies for the treatment of anxiety, obsessive-compulsive, and post-traumatic stress disorders in primary care

Antidepressants, Other

- Per the 2016 American College of Physicians (ACP) guidelines, treatment with either CBT or second-generation antidepressants for major depressive disorder (MDD) is recommended
- The 2009 American Psychiatric Association (APA) treatment guidelines recommend SSRIs, SNRIs, TCAs, and benzodiazepines as first-line pharmacotherapy for panic disorder
- Treatment-resistant depression (TRD) occurs in approximately 20% to 30% of patients with MDD

Antidepressants, Other

- Non-SSRI antidepressants are used as first-line therapy in children in the presence of comorbidities, such as attention-deficit/hyperactivity disorder (ADHD), where bupropion may be more effective than an SSRI
- All antidepressants have a boxed warning regarding suicidality in children, adolescents, and young adults
- Tranylcypromine (Parnate) carries a boxed warning informing that excessive consumption of foods or beverages that contain significant amounts of tyramine can precipitate hypertensive crisis

Antidepressants, Other

- Esketamine (Spravato) carries a boxed warning for risk of dissociation and sedation after administration as well as abuse and misuse
- Use of esketamine (Spravato) requires enrollment in the Spravato REMS program
- Pharmacotherapy should be selected based on adverse event profiles, co-morbidities, drug interactions, pharmacokinetics, patient preference, cost, and historical patient response
- For GAD, the International Consensus Group on Depression and Anxiety (ICGDA) recommends SSRIs, SNRIs, TCAs, and CBT as first-line treatments

Antidepressants, Other

- When response is inadequate with trial of a first-line therapy, strategies for treatment include maximizing the dose, switching to another class or another drug within the class, combination therapy, augmentation, or other nonpharmacologic therapy
- The Endocrine Society recommends SSRIs, SNRIs, gabapentin, or pregabalin for moderate to severe vasomotor symptoms (VMS) in patients with contraindications to hormone therapy or who choose not to use hormone therapy
- The American College of Obstetricians and Gynecologists (ACOG) also states SSRIs, SNRIs, clonidine, and gabapentin are effective alternatives to hormone therapy for the treatment of VMS related to menopause

Antidepressants, Other

- For the treatment perinatal depression, the American Congress of Obstetricians and Gynecologists (ACOG) recommends that SSRIs be used as first-line pharmacotherapy
- If the patient has been successfully treated previously with an antidepressant from any class, this should be the agent of choice
- They note that untreated depression during pregnancy is associated with disrupted health behaviors, relationships, parenting, and physiology
- The group acknowledges that the risks and benefits of psychopharmacotherapy for perinatal mental health conditions be discussed with the patient when clinically indicated
- Due to the date of publication, ACOG clinical practice guidelines do not address the role of zuranolone (Zurzuvae) in the management of postpartum depression (PPD)
- Zuranolone is the first oral medication indicated specifically for treating PPD in adults

Antidepressants, Other

Clinical and Product Updates

- October 2024- duloxetine (Cymbalta)
  - FDA announced that Eli Lilly made a business decision to discontinue marketing Cymbalta (20 mg, 30 mg and 60 mg)
  - Generics remain available

- November 2024- brexanolone (Zulresso)
  - Sage has announced that it will discontinue the manufacture of Zulresso 5 mg/mL solution

Antidepressants, SSRIs

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Antidepressants, SSRIs

Drug	Mfr	MDD	GAD	SAD	Panic Disorder	PTSD	OCD	PMDD	Bulimia Nervosa	VMS
citalopram (Celexa)	generic, Allergan	X	--	--	--	--	--	--	--	--
escitalopram (Lexapro)	generic, Allergan	X (≥ 12 years)	X (≥ 7 years)	--	--	--	--	--	--	--
fluoxetine	generic, Alvogen	X (≥ 8 years)	--	--	X	--	X (≥ 7 years)	--	X	--
fluoxetine (Prozac)	generic, Dista	X (≥ 8 years)	--	--	X	--	X (≥ 7 years)	--	X	--
fluoxetine DR	Dr. Reddy's	X	--	--	--	--	--	--	--	--
fluvoxamine	generic	--	--	--	--	--	X (≥ 8 years)	--	--	--
fluvoxamine ER	generic	--	--	--	--	--	X	--	--	--

Antidepressants, SSRIs

Drug	Mfr	MDD	GAD	SAD	Panic Disorder	PTSD	OCD	PMDD	Bulimia Nervosa	VMS
paroxetine HCl (Paxil)	generic, Apotex	X	X	X	X	X	X	--	--	--
paroxetine HCl controlled release (Paxil CR)	generic, Apotex	X	--	X	X	--	--	X	--	--
paroxetine mesylate	Solco, Padagis	--	--	--	--	--	--	--	--	X
paroxetine mesylate (Pexeva)	Sebela	X	X	--	X	--	X	--	--	--
sertraline	Almatica	X	--	--	--	--	X (≥ 6 years)	--	--	--
sertraline (Zoloft)	generic, Pfizer/ Viatris	X	--	X	X	X	X (≥ 6 years)	X	--	--

Antidepressants, SSRIs

- SSRIs are generally considered first-line therapy for their FDA-approved indications due to improved tolerability, lower lethality in overdose, safety in cardiovascular disease, and lesser incidence of weight gain
- SSRIs have comparable efficacy and adverse event profiles for their FDA-approved indications
- SSRIs are preferred as a first medication trial for OCD and are recommended first-line medications for the treatment of PTSD
- For social anxiety disorder, the ICGDA expert panel guidelines recommend SSRIs as first-line therapy

Antidepressants, SSRIs

- The 2020 American Academy of Child and Adolescent Psychiatry (AACAP) recommend SSRIs are first-line agents for the treatment of anxiety disorders in children 6-18 years old
- Fluoxetine (Prozac) is the only SSRI medication approved by the FDA for the treatment of bulimia and has been shown to reduce the episodes of binge-eating and purging behavior, and their chance of relapse
- It is recommended first-line in the 2023 APA eating disorder guidelines
- The American Association of Clinical Endocrinologists (AACE) states that therapeutic trials of SSRIs and possibly other nonhormonal medications may be considered for the relief of menopausal symptoms in women with no specific contraindications
- Paroxetine mesylate (Brisdelle) is the only SSRI approved to treat VMS

Antidepressants, SSRIs

Clinical and Product Updates

- October 2024- fluoxetine (Prozac)
  - Eli Lilly will be discontinuing brand-name Prozac capsules
  - Generics remain available

Antivirals, Topical

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Antivirals, Topical

Drug	Manufacturer	Indications
acyclovir cream (Zovirax)	generic, Bausch	Treatment of recurrent herpes labialis (cold sores) in immunocompetent adults and children 12 years of age and older
acyclovir ointment (Zovirax)	generic, Bausch	Management of initial genital herpes and in limited non-life-threatening mucocutaneous herpes simplex virus infections in immunocompromised adult patients
acyclovir/ hydrocortisone (Xerese)	Bausch	Early treatment of recurrent herpes labialis (cold sores) to reduce the likelihood of ulcerative cold sores and to shorten the lesion healing time in adults and children 6 years of age and older
docosanol (Abreva)	generic, GlaxoSmithKline	Treatment of cold sores/fever blisters on the face or lips in adults and children 12 years of age and older to shorten healing time and duration of symptoms
penciclovir (Denavir)	generic, Mylan	Treatment of recurrent herpes labialis (cold sores) in adults and children 12 years of age and older

Antivirals, Topical

- In the US, about 48% of people aged 14 to 49 years have serologic infection with HSV-1 and 12% are seropositive for HSV-2
- Approximately 80% of oral lesions are caused by HSV-1 and about 20% of genital lesions
- As much as 30% to 40% of genital herpes in adolescent patients is caused by HSV-1
- The HSV-1 and HSV-2 viruses become reactivated secondary to certain stimuli including fever, upper respiratory infection, physical or emotional stress, ultraviolet light exposure, and axonal injury
- Topical antiviral medications are used for the treatment of an active lesion and should be started during the prodrome phase, characterized by perioral tingling, itching, and redness, to be most beneficial
- Overall, acyclovir, penciclovir, and docosanol for herpes labialis treatment only provide modest benefit if used very early in the prodrome phase

Antivirals, Topical

- Compared to placebo, treatment has reduced lesion healing time by approximately 0.75 to 1.5 days in clinical trials
- Left untreated, herpes labialis may take up to 10 days or more to heal
- According to studies, all products are effective in treating herpes labialis and provide symptom relief, such as decreased lesion count, lesion size, pain, and healing time compared to placebo
- The 2021 Centers for Disease Control and Prevention (CDC) sexually-transmitted infections (STI) recommendations for genital herpes state oral antiviral therapy is preferred over topical antiviral therapy

Bone Resorption Suppression and Related Agents

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Bone Resorption Suppression and Related Agents

Drug	Manufacturer	Indications
Bisphosphonates		
alendronate (Binosto)	Ascend, Radius Health	Treatment of osteoporosis in postmenopausal women Treatment to increase bone mass in men with osteoporosis
alendronate (Fosamax)	generic, Organon	Treatment and prevention of osteoporosis in postmenopausal women Treatment to increase bone mass in men with osteoporosis Treatment of glucocorticoid-induced osteoporosis in men and women receiving glucocorticoids in a daily dosage equivalent of ≥ 7.5 mg of prednisone and who have low bone mineral density Treatment of Paget's disease of bone in men and women
alendronate/vitamin D (Fosamax Plus D)	Organon	Treatment of osteoporosis in postmenopausal women Treatment to increase bone mass in men with osteoporosis
ibandronate	generic	Treatment and prevention of osteoporosis in postmenopausal women
risedronate (Actonel)	generic, Actavis/Allergan	Treatment and prevention of osteoporosis in postmenopausal women Treatment to increase bone mass in men with osteoporosis Prevention and treatment of glucocorticoid-induced osteoporosis in men and women who are either initiating or continuing systemic glucocorticoids in a daily dosage equivalent of ≥ 7.5 mg of prednisone for chronic diseases Treatment of Paget's disease of bone in men and women
risedronate delayed-release (Atelvia)	generic, Actavis/Allergan	Treatment of osteoporosis in postmenopausal women

Bone Resorption Suppression and Related Agents

Drug	Manufacturer	Indications
Calcitonins		
calcitonin-salmon	generic	Treatment of postmenopausal osteoporosis in females > 5 years post menopause when alternative treatments are not suitable. Fracture reduction efficacy has not been demonstrated.
Others		
abaloparatide (Tymlos)	Radius Health	Treatment of osteoporosis in postmenopausal women who are at high risk for fracture, defined as a history of osteoporotic fracture or multiple risk factors for fracture, or in patients who have failed or are intolerant to other available osteoporosis therapy Treatment to increase bone density in men with osteoporosis at high risk for fracture, defined as a history of osteoporotic fracture or multiple risk factors for fracture, or in patients who have failed or are intolerant to other available osteoporosis therapy
denosumab (Prolia)	Amgen	Treatment of osteoporosis in postmenopausal women at high risk for fracture, defined as a history of osteoporotic fracture, or multiple risk factors for fracture, or in patients who have failed or are intolerant to other available osteoporosis therapy Treatment of osteoporosis associated with newly initiated or sustained systemic glucocorticoid therapy at a dose ≥ 7.5 mg daily of prednisone to be continued for at least 6 months in men and women at high risk for fracture Treatment of bone loss in men with prostate cancer on androgen deprivation therapy Treatment of bone loss in women undergoing breast cancer therapy with adjuvant aromatase inhibitor therapy Treatment to increase bone mass in men diagnosed with osteoporosis and a high fracture risk or in patients who have failed or are intolerant to other osteoporosis therapies

Bone Resorption Suppression and Related Agents

Drug	Manufacturer	Indications
Others (Cont'd)		
raloxifene (Evista)	generic, Eli Lilly	Treatment and prevention of osteoporosis in postmenopausal women Reduction in risk of invasive breast cancer in postmenopausal women who either have osteoporosis or are at high risk for invasive breast cancer
romosozumab-aqqg (Evenity)	Amgen	Treatment of osteoporosis in postmenopausal women at high risk for fracture, defined as a history of osteoporotic fracture, or multiple risk factors for fracture; or patients who have failed or are intolerant to other available osteoporosis therapy
teriparatide	Alvogen	Treatment of osteoporosis in postmenopausal women who are at high risk for fracture or who have failed or are intolerant to other available osteoporosis therapy Increase of bone mass in men with primary or hypogonadal osteoporosis who are at high risk for fracture or who have failed or are intolerant to other available osteoporosis therapy Treatment of men and women with osteoporosis associated with sustained systemic glucocorticoid therapy (daily dosage equivalent to ≥ 5 mg of prednisone) at high risk for fracture or who have failed or are intolerant to other available osteoporosis therapy
teriparatide (Forteo)	generic, Eli Lilly	Treatment of osteoporosis in postmenopausal women who are at high risk for fractures or who have failed or are intolerant to other available osteoporosis therapy Increase of bone mass in men with primary or hypogonadal osteoporosis who are at high risk for fractures or who have failed or are intolerant to other available osteoporosis therapy Treatment of men and women with osteoporosis associated with sustained systemic glucocorticoid therapy (daily dosage equivalent to ≥ 5 mg of prednisone) at high risk for fracture or who have failed or are intolerant to other available osteoporosis therapy

Bone Resorption Suppression and Related Agents

- Approximately 12 million Americans have a diagnosis of osteoporosis, and an additional 43 million have low bone mass, placing them at increased risk for this disease
- The American Association of Clinical Endocrinologists (AACE) and American College of Endocrinology (ACE) clinical practice guidelines for the diagnosis and treatment of postmenopausal osteoporosis (2020 update) recommend alendronate, risedronate, zoledronic acid, and denosumab as initial therapy for most patients at high risk of fracture
- Per the AACE/ACE, teriparatide, abaloparatide, denosumab, romosozumab, or zoledronic acid should be considered for patients unable to use oral therapy and as initial therapy for patients at especially high fracture risk

Bone Resorption Suppression and Related Agents

- The Bone Health & Osteoporosis Foundation (BHOF) Clinician's Guide to prevention and treatment of osteoporosis recommends a "treat-to-target" approach to therapy that includes a specific BMD goal and no fractures
- The guide states that a therapy proven to reduce the risk of both vertebral and non-vertebral fractures (e.g., alendronate, risedronate, zoledronic acid, denosumab, teriparatide, abaloparatide, romosozumab) should be considered preferentially over a therapy that has not demonstrated vertebral and non-vertebral fracture risk reduction (e.g., raloxifene, calcitonin, ibandronate)
- Combination therapy with an anabolic agent (e.g., teriparatide, abaloparatide) and an anti-resorptive agent (e.g., bisphosphonate, denosumab) may be warranted for a patient at very high risk for fracture (e.g., multiple vertebral fractures)
- Calcitonin salmon should be reserved as second-line treatment for postmenopausal women when other drug therapies are not suitable

Bone Resorption Suppression and Related Agents

- In 2023, the American College of Physicians (ACP) published an update to the 2017 guidelines for the treatment of low bone mass and primary osteoporosis to prevent fractures in adults
- ACP recommends physicians offer bisphosphonates for initial treatment of postmenopausal women with primary osteoporosis to reduce the risk of fractures and men with primary osteoporosis
- Denosumab is suggested second-line as an option in postmenopausal women or men with primary osteoporosis for whom bisphosphonates are not appropriate or who experience adverse effects with bisphosphonates
- In postmenopausal women with a very high risk of fracture, ACP suggests romosozumab or teriparatide followed by a bisphosphonate

Bone Resorption Suppression and Related Agents

- According to the American College of Rheumatology's (ACR) 2017 updated guidance on managing glucocorticoid-induced osteoporosis in adults and children, treatment should include optimal calcium and vitamin D intake and lifestyle changes consistent with good bone health
- ACR's recommendations on antiresorptive treatment are based on individual patient characteristics, including fracture risk, age, and special populations
- In patients with moderate to high risk of fracture, oral bisphosphonates are generally recommended as first-line therapy, per ACR; subsequent treatments may include IV bisphosphonates, teriparatide, denosumab, and raloxifene

Bone Resorption Suppression and Related Agents

- The Endocrine Society 2020 guidelines on osteoporosis recommends pharmacologic therapy for postmenopausal women at high risk of fracture, especially those with recent fracture
- These patients should be treated initially with a bisphosphonate or denosumab to reduce fracture risk; however, ibandronate is not recommended to reduce the risk of nonvertebral or hip fracture
- Denosumab is an alternative initial agent for patients at high risk of fracture
- For postmenopausal women with a very high risk of fracture, these guidelines recommend starting with either teriparatide or abaloparatide for up to 2 years of treatment before switching to a bisphosphonate or denosumab to maintain bone density

Bone Resorption Suppression and Related Agents

- These guidance also included Evenity, which was concluded to be a potential treatment option for select postmenopausal women at very high risk of fracture, but patients should be carefully evaluated due to the serious potential cardiovascular events
- After completing a course of romosozumab-aqqg, it is recommended that patients receive treatment with antiresorptive therapies to maintain gains in bone density and reductions in fracture risk
- Raloxifene may be considered in patients with a low risk of deep vein thrombosis and a high risk of breast cancer.
- Calcitonin is only recommended if patients cannot tolerate or are not appropriate candidates for treatment with other therapies

Bone Resorption Suppression and Related Agents

- The North American Menopause Society (NAMS) updated their recommendations for osteoporosis prevention and management in postmenopausal women
- In addition to nonpharmacologic treatments, supplements, and lifestyle modifications, the pharmacologic treatment should be based on the current BMD and fracture risk
- Raloxifene is recommended for the treatment of postmenopausal osteoporosis in women with a low risk of hip fracture, an elevated risk of breast cancer, and low risk of stroke and VTE

Bone Resorption Suppression and Related Agents

- Bisphosphonates to reduce fracture risk in women with postmenopausal osteoporosis
- Denosumab for women with postmenopausal osteoporosis, including those at high risk of fracture
- Osteoanabolic therapies in women at very high risk of fracture, including those with prior/recent fractures, very low BMD (T-score below −3.0), and those who sustain fractures or lose BMD while taking anti-remodeling therapy

Bone Resorption Suppression and Related Agents

Clinical and Product Updates

- January 2024
  - FDA released a Drug Safety Communication to warn that denosumab (Prolia) increases the risk of severe hypocalcemia in patients with advanced CKD including dialysis-dependent patients
  - Cases of serious harm, including hospitalization, life-threatening events, and death have been reported
  - Severe hypocalcemia is more common in patients with CKD who also have mineral and bone disorder (CKD-MBD)
  - In patients with advanced CKD taking denosumab, severe hypocalcemia

Bone Resorption Suppression and Related Agents

Clinical and Product Updates

- March 2024
  - FDA has approved denosumab-bbdz (Wyost) as a new interchangeable biosimilar to denosumab (Xgeva)
  - Wyost is approved for:
    - (1) Prevention of skeletal-related events in pts with multiple myeloma & in patients with bone metastases from solid tumors
    - (2) Treatment of adults & skeletally mature adolescents with giant cell tumor of bone that is unresectable or where surgical resection is likely to result in severe morbidity
    - (3) Treatment of hypercalcemia of malignancy refractory to bisphosphonate treatment
  - Recommended dosage is 120 mg SC every 4 weeks; additional 120 mg doses should be given on days 8 & 15 of the first month of treatment for giant cell tumor of bone & hypercalcemia of malignancy
  - Product will be available as 70 mg/mL solution for injection in an SDV

Bone Resorption Suppression and Related Agents

Clinical and Product Updates

- March 2024
  - FDA has approved denosumab-bbdz (Jubbonti) as a new interchangeable biosimilar to denosumab (Prolia)
  - Jubbonti is approved for:
    - (1) Treatment of postmenopausal women with osteoporosis at high risk for fracture
    - (2) Treatment to increase bone mass in men with osteoporosis at high risk for fracture
    - (3) Treatment of glucocorticoid-induced osteoporosis
    - (4) Treatment to increase bone mass in men at high risk for fracture receiving androgen deprivation treatment for nonmetastatic prostate cancer
    - (5) Treatment to increase bone mass in women at high risk for fracture receiving adjuvant aromatase inhibitor treatment for breast cancer
  - Recommended dosage for all indications is 60 mg SC every 6 months administered by an HCP
  - Product will be available as 60 mg/mL solution for injection in a single-dose PFS
  - Jubbonti approval includes a REMS program

Bone Resorption Suppression and Related Agents

Clinical and Product Updates

- June 2024
  - The FDA has approved teriparatide injection, a parathyroid hormone analog indicated for
    - (1) Treatment of postmenopausal women with osteoporosis at high risk for fracture or patients who have failed or are intolerant to other available osteoporosis therapy
    - (2) Increase of bone mass in men with primary or hypogonadal osteoporosis at high risk for fracture or patients who have failed or are intolerant to other available osteoporosis therapy;
    - (3) Treatment of men and women with osteoporosis associated with sustained systemic glucocorticoid therapy at high risk for fracture or patients who have failed or are intolerant to other available osteoporosis therapy
  - Supplied in a single-patient-use prefilled pen (600 mcg/2.4 mL) that contains 28 daily doses of 20 mcg
  - Recommended dosage is 20 mcg SC once daily into the thigh or abdominal region; calcium and vitamin D should be considered based on individual patient need
  - Use of teriparatide for > 2 years should only be considered for pts at or who return to a high fracture risk

Bronchodilators, Beta Agonists

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Bronchodilators, Beta Agonists

Class Overview: Long-Acting Agents

- aformoterol tartrate - (Brovana Solution)
- formoterol fumarate - (Perforomist Solution)
- olodaterol HCl - (Striverdi Respimat)
- salmeterol - (Serevent Diskus)

Bronchodilators, Beta Agonists

Class Overview: Nebulized Agents

- albuterol sulfate - (AccuNeb; albuterol neb soln 0.63mg & 1.25mg, 2.5mg/0.5ml, 2.5mg/3ml & 5mg/ml)
- levalbuterol HCl - (levalbuterol neb soln; levalbuterol neb soln conc; Xopenex Neb Soln)

Bronchodilators, Beta Agonists

Class Overview: Oral Agents

- albuterol sulfate - (albuterol ER, syrup & tablet)
- terbutaline sulfate - (terbutaline)

Class Overview: Short-Acting Agents

- albuterol sulfate - (ProAir Digihaler; ProAir HFA; ProAir Respiclick; Proventil HFA; Ventolin HFA)
- levalbuterol tartrate - (Xopenex HFA)

Bronchodilators, Beta Agonists

- Prevalence and incidence of asthma in the U.S is approximately 7.7% of adults and 6.5% of children, as of 2021
- It is estimated that the number of Americans with a COPD diagnosis is approximately 16 million
- Beta2-agonist bronchodilators are used for the treatment and prevention of bronchospasm associated with asthma, prophylaxis of exercise-induced bronchospasm (EIB), and in the treatment of Chronic Obstructive Lung Disease (COPD)
- Mainstay of asthma therapy is the use of inhaled corticosteroids (ICS) alone or in combination with long-acting beta2-agonists (LABAs) as controller medications

Bronchodilators, Beta Agonists

- These agents lead to improvements in symptoms, reducing the need for short-acting beta2-agonists (SABAs) for quick relief
- Due to the increased risk of severe exacerbations with regular or frequent use, short-acting beta agonist (SABA)-only treatment is no longer recommended
- For most asthma patients, treatment can be initiated with an as-needed low dose ICS-formoterol, daily low dose ICS, or low dose ICS taken whenever a SABA is taken

Bronchodilators, Beta Agonists

- Delivery system selection as well as the patients' ability to properly use the device are important factors in the clinical success of bronchodilator therapy
- Metered dose inhalers (MDIs) are pressurized spray inhalers, available in suspension and solution
- Spacer chambers may be used with most MDIs to make them easier to use and help deliver a greater amount of medicine to the airway
- Dry-powder inhalers (DPIs) are breath-actuated devices that release the medicine in the form of a dry powder upon inhalation

Bronchodilators, Beta Agonists

- Nebulizers, may be the only viable alternative delivery system for certain children and those unable to use inhalers due to the inability to synchronize breaths and device actuation
- Some delivery devices, (like Respimat devices), are not breath-activated, but still require coordination of actuation and inhalation
- Oral dosage forms of albuterol are less utilized than the inhaled forms due to systemic beta-adrenergic stimulation, especially in patients sensitive to these effects, such as those with cardiovascular disease
- Levalbuterol has similar efficacy to albuterol and there are no significant differences in adverse effects

Bronchodilators, Beta Agonists

- In May 2019, the FDA removed the boxed warning from the labeling for indacaterol (Arcapta Neohaler), arformoterol (Brovana), formoterol (Perforomist), and olodaterol (Striverdi)
- The warning remains in the labeling of salmeterol (Serevent Diskus) - a boxed warning about a small, but significant, increased risk of life-threatening asthma episodes or asthma-related deaths when used as monotherapy

Bronchodilators, Beta Agonists

- In August 2020, Choosing Wisely, an initiative of the American Board of Internal Medicine (ABIM), released guidance for the management of pediatric asthma based on information from the American Academy of Pediatrics
- They recommend a thorough evaluation of medication adherence, technique, and device appropriateness prior to stepping up asthma therapy in this patient population
- The guidance recommends against the use of LABA/ICS combination inhalers as initial therapy in pediatric patients with intermittent or mild persistent asthma
- They state that typically a single agent, such as a low-dose ICS or leukotriene modifier, is sufficient to maintain asthma control

Bronchodilators, Beta Agonists

- In 2020, the American Thoracic Society (ATS) released additional guidelines for the pharmacologic management of COPD
- The panel strongly recommends the use of dual LABA/LAMA therapy over LABA or LAMA monotherapy in COPD patients who complain of exercise intolerance or dyspnea
- In patients who complain of dyspnea or exercise intolerance despite dual therapy with LABA/LAMA, the ATS suggests triple therapy (ICS/LABA/LAMA) in patients with a history of ≥ 1 exacerbations requiring hospitalization, oral steroids, or antibiotics in the past year

Bronchodilators, Beta Agonists

- The ATS recommends against maintenance oral corticosteroid therapy in patients with frequent and severe exacerbations while on optimal therapy
- For patients receiving triple combination therapy who experience no exacerbations over the course of 1 year, the ATS suggests that ICS therapy may be discontinued

Bronchodilators, Beta Agonists

- The 2024 GOLD guidelines place a great focus on the assessment of inhaler technique and adherence to improve therapeutic outcomes
- The NAEPP Expert Panel Report-3 (EPR-3) report released in 2007 by the National Heart, Lung, and Blood Institute (NHLBI) also recommends a similar classification of asthma severity and control to guide in the initiation and adjustment of therapy
- A focused update to these guidelines was released in 2020
- As needed ICS with formoterol is recommended instead for patients 5 to 11 years of age at steps 3 and 4 (as low-dose or medium-dose, respectively); a SABA is recommended as an alternative
- For combinations of an ICS and a LABA for patients ≥ 5 years of age, the group states a single inhaler is preferable

Bronchodilators, Beta Agonists

2024 GOLD Guidelines:

Assessment of Airflow Limitation:

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

Assessment of Exacerbation Risk and Symptoms:

		Symptoms	
Moderate or Severe Exacerbation History		mMRC grade 0 to 1; CAT< 10	mMRC grade ≥ 2; CAT ≥ 10
	0 to 1 moderate exacerbations per year (not leading to hospitalization)	Group A	Group B
	≥ 2 moderate exacerbations per year or ≥ 1 exacerbation leading to hospitalization	Group E	

Bronchodilators, Beta Agonists

- ## Global Initiative for Asthma (GINA), 2023
  - 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

Bronchodilators, Beta Agonists

Global Initiative for Asthma (GINA), 2023

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 or **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)

Bronchodilators, Beta Agonists

Global Initiative for Asthma (GINA), 2023

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 or **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)

Bronchodilators, Beta Agonists

Clinical and Product Updates

- May 2024
  - Teva will discontinue the manufacture of ProAir Digihaler 90 mcg metered powder inhaler

Gaucher Disease

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Gaucher Disease

FDA-Approved Indications and Dosages

Drug	Manufacturer	Indication(s)	Dosage	Availability
Enzyme Replacement Therapy (ERT)				
imiglucerase (Cerezyme®)[1]	Genzyme	Long-term enzyme replacement therapy for pediatric patients (≥ 2 years of age) and adults with confirmed type 1 Gaucher disease that results in ≥ 1 of the following conditions: ▪ anemia ▪ thrombocytopenia ▪ bone disease ▪ hepatomegaly or splenomegaly	Individualized dosing by intravenous (IV) infusion; 2.5 units/kg of body weight 3 times/week up to 60 units/kg every 2 weeks Initial dosages range from 2.5 units/kg of body weight 3 times a week to 60 units/kg once every 2 weeks; most data available with 60 units/kg every 2 weeks	Lyophilized powder for injection (single-use): ▪ 400 units/vial
taliglucerase alfa (Elelyso®)[2]	Pfizer	Long-term enzyme replacement therapy for adults and pediatric patients (≥ 4 years of age) with confirmed type 1 Gaucher disease	Treatment-naïve adult and pediatric patients ≥ 4 years of age: 60 units/kg every other week as a 60-to-120-minute IV infusion For patients switching from imiglucerase, start taliglucerase at the same unit/kg dose as the patient's previous imiglucerase dose Dosage adjustments can be made based on patient achieving as well as maintaining individual therapeutic goals	Lyophilized powder for injection (single-use): ▪ 200 units/vial

Gaucher Disease

FDA-Approved Indications and Dosages (continued)

Drug	Manufacturer	Indication(s)	Dosage	Availability
Enzyme Replacement Therapy (ERT) *(continued)*				
velaglucerase alfa (Vpriv®)[3]	Shire Human Genetic Therapies	Long-term enzyme replacement therapy for pediatric patients (≥ 4 years of age) and adults with type 1 Gaucher disease	Individualized dosing by 60-minute IV infusion; 60 units/kg administered every 2 weeks; trials have evaluated doses from 15 units/kg to 60 units/kg every other week[4] Patients being treated with stable imiglucerase dosages for Gaucher disease can switch to velaglucerase at previous imiglucerase dose 2 weeks after last imiglucerase dose	Lyophilized powder for injection (single-use): ▪ 400 units/vial
Substrate Reduction Therapy				
eliglustat (Cerdelga®)[5]	Genzyme	Treatment of adult patients with type 1 Gaucher disease who are CYP2D6 extensive metabolizers, intermediate metabolizers, or poor metabolizers as detected by an FDA-approved test*	Extensive or intermediate CYP2D6 metabolizers: 84 mg twice daily Poor CYP2D6 metabolizers: 84 mg once daily	Capsule: 84 mg
miglustat (Yargesa, Zavesca®)[6,7]	generic, Edenbridge, Actelion	Treatment of adult patients with mild to moderate type 1 Gaucher disease for whom enzyme replacement therapy is not a therapeutic option (e.g., due to constraints such as allergy, hypersensitivity, or poor venous access)	100 mg three times daily; reduce frequency to once or twice daily if adverse effects (diarrhea or tremor) become problematic	Capsule: 100 mg

Gaucher Disease

- Gaucher disease (GD) is an autosomal recessive condition caused by deficiency of glucocerebrosidase
- This deficiency results in abnormal accumulation of glycolipids in cell lysosomes, which can lead to skeletal disease , anemia, hemorrhage, thrombocytopenia, splenomegaly, hepatomegaly, and growth retardation
- All IV enzyme replacement therapy (ERT) agents, imiglucerase (Cerezyme), velaglucerase alfa (Vpriv), and taliglucerase alfa (Elelyso) are forms of the enzyme glucocerebrosidase, whereas oral substrate reduction therapy (SRT) agents, eliglustat (Cerdelga) and miglustat (Zavesca), function as competitive and reversible inhibitors of the enzyme glucosylceramide synthase

Gaucher Disease

- The International Collaborative Gaucher Group (ICGG) Gaucher Registry guidelines developed from a consensus of international experts recommend ERT for symptomatic pediatric patients and for those with severe disease
- Treatment should be individualized as response may vary
- Treatment is life-long, and therapy interruptions are not recommended
- Anaphylaxis has been reported in patients treated with taliglucerase
- The use of miglustat has been limited due to toxicity
- Data demonstrate that Cerezyme use is not associated with an increased risk of major birth defects, miscarriage, or other adverse maternal or fetal outcomes

Erythropoiesis Stimulating Proteins

ARIZONA HEALTH CARE COST CONTAINMENT SYSTEM

Erythropoiesis Stimulating Proteins

FDA-Approved Indications

Drug	Manufacturer	FDA-approved Indications
daprodustat (Jesduvroq)[1]	GlaxoSmithKline	▪ Treatment of anemia due to chronic kidney disease (CKD) in adults who have been receiving dialysis for ≥ 4 months – Daprodustat has not been shown to improve quality of life, fatigue, or patient well-being – Daprodustat is not indicated for use as a substitute for red blood cell (RBC) transfusion in patients requiring immediate correction of anemia – Daprodustat is not indicated for use in patients who are not on dialysis
darbepoetin (Aranesp®)[2]	Amgen	▪ Treatment of anemia associated with CKD including patients on dialysis and patients not on dialysis ▪ Treatment of anemia in patients with non-myeloid malignancies where anemia is due to the effect of concomitant myelosuppressive chemotherapy and, upon initiation, a minimum of 2 additional months of chemotherapy is planned – Darbepoetin is not indicated for patients receiving myelosuppressive therapy when the anticipated outcome is cure or in in whom anemia can be managed by transfusion – Darbepoetin is not indicated for use in patients receiving hormonal agents, therapeutic biologic products, or radiotherapy unless receiving concomitant myelosuppressive chemotherapy – Darbepoetin is not indicated as a substitute for RBC transfusion in patients who require immediate correction of anemia – Darbepoetin use has not been demonstrated in controlled clinical trials to improve quality of life, fatigue, or patient well-being
luspatercept-aamt (Reblozyl®)[3]	Celgene/BMS	▪ Treatment of anemia in adult patients with beta thalassemia who require regular RBC transfusions ▪ Treatment of anemia without previous erythropoiesis stimulating agent (ESA) use (ESA-naïve) in adults with very low- to intermediate-risk myelodysplastic syndromes (MDS) who may require regular RBC transfusions ▪ Treatment of anemia failing an ESA and requiring ≥ 2 RBC units over 8 weeks in adult patients with very low- to intermediate-risk MDS with ring sideroblasts (MDS-RS) or with myelodysplastic/myeloproliferative neoplasm with ring sideroblasts and thrombocytosis (MDS/MPN-RS-T) – Luspatercept-aamt is not indicated for use as a substitute for RBC transfusions in patients who require immediate correction of anemia

Erythropoiesis Stimulating Proteins

Drug	Manufacturer	FDA-approved Indications
PEG-EPO (Mircera®)[4]	Vifor	▪ Treatment of anemia associated with CKD in adult patients on dialysis and adult patients not on dialysis ▪ Treatment of anemia associated with CKD in pediatric patients 3 months to 17 years of age on dialysis or not on dialysis who are converting from another ESA after their hemoglobin (Hb) level was stabilized with an ESA – PEG-EPO use has not been demonstrated in controlled clinical trials to improve quality of life, fatigue, or patient well-being – PEG-EPO is not indicated for treatment of anemia due to cancer chemotherapy – PEG-EPO is not indicated as a substitute for RBC transfusion in patients who require immediate correction of anemia

Erythropoiesis Stimulating Proteins

Drug	Manufacturer	FDA-approved Indications
rHuEPO (Epogen®)[5]	Amgen	▪ Treatment of anemia associated with CKD including patients on dialysis and patients not on dialysis to decrease the need for RBC transfusion ▪ Treatment of anemia related to therapy with zidovudine (≤ 4,200 mg per week) in HIV-infected patients with endogenous serum erythropoietin levels of ≤ 500 mUnits/mL ▪ Treatment of anemia in patients with non-myeloid malignancies where anemia is due to the effect of concomitant myelosuppressive chemotherapy and, upon initiation, Hb < 10 g/dL and there is a minimum of 2 additional months of planned chemotherapy ▪ Indicated to reduce the need for allogeneic RBC transfusion among patients with perioperative Hb > 10 to ≤ 13 g/dL who are at high risk for perioperative blood loss from elective, noncardiac, nonvascular surgery – rHuEPO is not indicated for use in patients receiving hormonal agents, therapeutic biologic products, or radiotherapy unless receiving concomitant myelosuppressive chemotherapy – rHuEPO is not indicated for patients receiving myelosuppressive therapy when the anticipated outcome is cure or in in whom anemia can be managed by transfusion – rHuEPO is not indicated as a substitute for RBC transfusion in patients who require immediate correction of anemia – rHuEPO is not indicated in patients undergoing cardiac or vascular surgery – rHuEPO is not indicated for patients who are willing to donate autologous blood pre-operatively – rHuEPO use has not been demonstrated in controlled clinical trials to improve quality of life, fatigue, or patient well-being
rHuEPO (Procrit®)[6]	Amgen (distributed by Janssen)	

Erythropoiesis Stimulating Proteins

Drug	Manufacturer	FDA-approved Indications
rHuEPO-epbx[z] (Retacrit®)[7]	Pfizer (Hospira), Vifor	▪ Treatment of anemia associated with CKD including patients on dialysis and patients not on dialysis to decrease the need for RBC transfusion ▪ Treatment of anemia due to zidovudine administered at ≤ 4,200 mg per week in HIV-infected patients with endogenous serum erythropoietin levels of ≤ 500 mUnits/mL ▪ Treatment of anemia in patients with non-myeloid malignancies where anemia is due to the effect of concomitant myelosuppressive chemotherapy and, upon initiation, there is a minimum of 2 additional months of planned chemotherapy ▪ Reduce the need for allogeneic RBC transfusions among patients with perioperative Hb > 10 to ≤ 13 g/dL who are at high risk for perioperative blood loss from elective, noncardiac, nonvascular surgery – Epoetin alfa-epbx is not indicated for use in patients receiving hormonal agents, therapeutic biologic products, or radiotherapy unless receiving concomitant myelosuppressive chemotherapy – Epoetin alfa-epbx is not indicated for patients receiving myelosuppressive therapy when the anticipated outcome is cure or in in whom anemia can be managed by transfusion – Epoetin alfa-epbx is not indicated as a substitute for RBC transfusion in patients who require immediate correction of anemia – Epoetin alfa-epbx is not indicated in patients undergoing cardiac or vascular surgery – Epoetin alfa-epbx is not indicated for patients who are willing to donate autologous blood pre-operatively – Epoetin alfa-epbx use has not been demonstrated in controlled clinical trials to improve quality of life, fatigue, or patient well-being

Erythropoiesis Stimulating Proteins

- A frequent complication, affecting over 3 million Americans
- Associated with serious diseases, such as chronic kidney disease (CKD), diabetes, heart disease, and cancer, as well as chronic inflammatory conditions like rheumatoid arthritis or inflammatory bowel disease
- Erythropoietin is a glycoprotein produced in the kidneys that stimulates RBC production from bone marrow. Acts on the erythroid progenitor cells in the bone marrow to cause late differentiation and maturity of the RBCs
- Endogenous production of erythropoietin by the kidney is normally regulated by the level of tissue oxygenation
- Hypoxia and anemia generally increase the production of erythropoietin, which in turn stimulates erythropoiesis
- In normal subjects, plasma erythropoietin levels range from 0.01 to 0.03 units/mL and may increase 100- to 1,000-fold during hypoxia or anemia. However, patients with CKD have impaired production of erythropoietin, which is the primary cause of their anemia

Erythropoiesis Stimulating Proteins

Beta thalassemia

- A rare inherited blood disorder marked by the reduction of functional hemoglobin levels, has an incidence of approximately 1 in 100,000 individuals in the general population
- There are 3 subtypes of beta thalassemia, which are characterized by the severity of symptoms – minor, intermedia, and major
- Individuals with beta thalassemia major require regular blood transfusions, as often as once every 2 to 4 weeks and are dependent on medical care for survival

Treatment for beta thalassemia

- Highly dependent on type of thalassemia, progression and severity of disease, and the presence or absence of certain symptoms
- Treatment options may include regular blood transfusions, chelation therapy, folic acid treatment, removal of the spleen and/or gallbladder, and bone marrow transplantation

Luspatercept-aamt (Reblozyl)

- The first FDA-approved erythroid maturation agent, which reduces patient transfusion burden by regulating late-stage RBC maturation
- Approved for the treatment of anemia in adult patients with beta thalassemia who require regular red blood cell transfusions

Erythropoiesis Stimulating Proteins

- The updated American Society of Clinical Oncology (ASCO) and the American Society of Hematology (ASH) joint clinical practice guidelines for the use of ESAs in patients with cancer recommend minimizing ESA use, particularly in patients with malignancy being treated with curative intent

Erythropoiesis Stimulating Proteins

- The National Comprehensive Cancer Network (NCCN) guidelines state that erythropoiesis stimulating agents (ESAs) are associated with an increased risk of thrombosis, decreased survival, and shortened time to tumor
- Therefore, it is advised to use the lowest ESA dose possible to maintain hemoglobin (Hb) levels sufficient to avoid blood transfusions
- ESAs should not be administered outside of the treatment period

Erythropoiesis Stimulating Proteins

- ESAs may be offered to patients with chemotherapy-associated anemia whose cancer treatment is not curative in intent and whose hemoglobin level is < 10 g/dL
- The guideline recommends against the use of ESAs for the treatment of anemia associated with malignancy in patients who are not receiving concurrent myelosuppressive chemotherapy, except for patients with lower risk of myelodysplastic syndrome to avoid transfusions
- Therapy with Epogen/Procrit, Mircera, and Aranesp for CKD should not exceed target hemoglobin of greater than 11 g/dL

Erythropoiesis Stimulating Proteins

- The ASCO and ASH Update Committee maintains that all ESAs are equivalent with respect to effectiveness and safety
- The international Kidney Disease: Improving Global Outcomes (KDIGO) group 2012 guidelines state that each ESA is effective in achieving and maintaining target Hb levels
- Patients with endogenous serum erythropoietin levels ≤ 500 mUnits/mL, and who are receiving a dose of zidovudine ≤ 4,200 mg/week, may respond to rHuEPO therapy
- Patients with endogenous serum erythropoietin levels > 500 mUnits/mL do not appear to respond to rHuEPO therapy

Erythropoiesis Stimulating Proteins

- In 2011, the FDA published a safety communication regarding a more conservative dosing approach to ESAs in patients with CKD due to increased risks of cardiovascular (CV) events
- Retacrit is the first FDA-approved biosimilar to Epogen/Procrit; Retacrit is neither considered interchangeable with nor does it carry the same indications as the reference products
- Luspatercept-aamt (Reblozyl) is the first FDA-approved erythroid maturation agent, which reduces patient transfusion burden by regulating late-stage RBC maturation
- It is approved for the treatment of anemia in adult patients with beta thalassemia who require regular red blood cell transfusions

Erythropoiesis Stimulating Proteins

Product Update:

- FDA approved Vafseo (vadadustat), the hypoxia-inducible factor prolyl hydroxylase (HIF-PH) inhibitor, for the treatment of anemia due to chronic kidney disease (CKD) in adults who have been receiving dialysis for ≥ 3 months
  - It has not been shown to improve quality of life, fatigue, or patient well-being
  - It's not indicated for use:
    (1) As a substitute for transfusion in patients requiring immediate correction of anemia
    (2) In patients with anemia due to CKD not on dialysis
- Approved as 150 mg, 300 mg, and 450 mg tablets
- Recommended starting dose is 300 mg orally once daily, with or without food
  - Adjust dose to target Hb levels of 10 g/dL to 11 g/dL
  - Doses may range from 150 mg to a max of 600 mg
- Boxed warning for increased risk of death, MI, stroke, VTE, and vascular access thrombosis

Erythropoiesis Stimulating Proteins

Product Update:

- FDA has approved Mircera for the treatment of anemia associated with CKD in pediatric patients 3 months to 17 years of age on dialysis & not on dialysis who are converting from another erythropoiesis-stimulating agent (ESA) after their hemoglobin (Hb) level was stabilized on an ESA
  - Mircera had previously been approved for pediatric patients 5 to 17 years of age with CKD on hemodialysis, as well as adults on dialysis & not on dialysis
- A new SC route of administration for pediatric patients has also been added to labeling (previously, only option was IV route)
- Mircera should be administered every 4 weeks for pediatric patients
- Starting dose is calculated based on total weekly ESA dose at time of conversion, and dosing adjustments should be made based on Hb response

Erythropoiesis Stimulating Proteins

Product Update:

- GlaxoSmithKline has made a business decision to discontinue Jesduvroq (daprodustat)

Hypoglycemics, Alpha-Glucosidase Inhibitors

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Hypoglycemics, Alpha-Glucosidase Inhibitors

Class Overview:

- acarbose – Precose, acarbose
- miglitol – Glycet, miglitol

Hypoglycemics, Alpha-Glucosidase Inhibitors

- Indicated as adjunct to diet and exercise to improve glycemic control in patients with type 2 diabetes
- Miglitol is more potent than acarbose on a milligram-to-milligram basis
- Alpha glucosidase inhibitors only have a modest effect on lowering HbA1c by about 0.4 to 0.7 percent
- Alpha glucosidase inhibitors are relatively safe but GI side effects (e.g., bloating, flatulence, diarrhea) limit their use

Hypoglycemics, Metformins

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Hypoglycemics, Metformins

FDA-Approved Indications

Drug	Manufacturer	Indications
glipizide/ metformin (Metaglip™)[1]	generic	▪ Initial therapy to improve glycemic control in adults with type 2 diabetes as an adjunct to diet and exercise ▪ Second-line therapy in type 2 diabetics who have not achieved adequate glycemic control with a sulfonylurea or metformin alone
glyburide/ metformin (Glucovance®)[2]	generic	▪ Initial therapy to improve glycemic control in adults with type 2 diabetes as an adjunct to diet and exercise ▪ Second-line therapy in type 2 diabetics who have not achieved adequate glycemic control with a sulfonylurea or metformin alone ▪ In combination with a TZD in patients who do not have adequate glycemic control with Glucovance alone
metformin (Glucophage®)[3]	generic	▪ Improvement of glycemic control in adults with type 2 diabetes as an adjunct to diet and exercise in patients 10 years of age and older (including in combination with a sulfonylurea or insulin)
metformin ER (Fortamet™)[4]	Shionogi Pharma	▪ Improvement of glycemic control in adults with type 2 diabetes as an adjunct to diet and exercise
metformin ER (Glumetza™)[5]	Depomed	▪ Improvement of glycemic control in adults with type 2 diabetes as an adjunct to diet and exercise (including in combination with a sulfonylurea or insulin)
metformin XR (Glucophage XR®)[6]	generic	▪ Improvement of glycemic control in adults with type 2 diabetes as an adjunct to diet and exercise (including in combination with a sulfonylurea or insulin)
metformin oral solution (Riomet™)[7]	Sun	▪ Improvement of glycemic control in patients 10 years of age and older with type 2 diabetes as an adjunct to diet and exercise (including in combination with a sulfonylurea or insulin for ages 17 and older)
metformin ER oral suspension (Riomet ER™)[8]	Sun	▪ Improvement of glycemic control in patients 10 years of age and older with type 2 diabetes as an adjunct to diet and exercise

Hypoglycemics, Metformins

- 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
- The 2022 American Association of Clinical Endocrinology (AACE) updated guidelines recommend metformin as preferred initial therapy, in general

Hypoglycemics, Metformins

- Per the 2022 Kidney Disease Improving Global Outcomes (KDIGO) guidelines on managing patients with diabetes and CKD, metformin is first-line treatment in most patients with estimated glomerular filtration rate (eGFR) ≥ 30 mL/min/1.73 m^2
- 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

Hypoglycemics, Metformins

- Metformin-containing products should not be used in patients with:
  - Renal disease or severe renal dysfunction (estimated glomerular filtration rate
  - [eGFR] below 30 mL/minute/1.73 m2)
  - Acute or chronic metabolic acidosis including diabetic ketoacidosis
  - Conditions that can lead to renal dysfunction, including acute myocardial infarction and septicemia

Hypoglycemics, SGLT2

ARIZONA
HEALTH CARE COST
CONTAINMENT SYSTEM

Hypoglycemics, SGLT2

FDA-Approved Indications

Drug	Manufacturer	Indications
canagliflozin (Invokana®)[1]	Janssen	▪ Adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus (T2DM) ▪ To reduce the risk of major adverse cardiovascular events (MACE) in adults with T2DM and established cardiovascular disease (CVD) ▪ To reduce the risk of end-stage renal disease (ESRD), doubling of serum creatinine, cardiovascular (CV) death, and hospitalization for heart failure (HF) in adults with T2DM and diabetic nephropathy with albuminuria > 300 mg/day
canagliflozin/ metformin (Invokamet®)[2]	Janssen	▪ Adjunct to diet and exercise to improve glycemic control in adults with T2DM ▪ To reduce the risk of MACE in adults with T2DM and established CVD ▪ Canagliflozin is indicated: – To reduce the risk of MACE in adults with T2DM and established CVD – To reduce the risk of ESRD, doubling of serum creatinine, CV death, and hospitalization for HF in adults with T2DM and diabetic nephropathy with albuminuria
canagliflozin/ metformin ER (Invokamet® XR)[3]	Janssen	
dapagliflozin (Farxiga®)[4]	AstraZeneca	▪ Adjunct to diet and exercise to improve glycemic control in adults with T2DM ▪ To reduce the risk of hospitalization for HF in adults with T2DM and established CVD or multiple CV risk factors ▪ To reduce the risk of CV death, hospitalization for HF, and urgent HF visit in adults with HF ▪ To reduce the risk of sustained estimated glomerular filtration rate (eGFR) decline, ESRD, CV death, and hospitalization for HF in adults with chronic kidney disease (CKD) at risk of progression
dapagliflozin/ metformin ER (Xigduo® XR)[5]	AstraZeneca	▪ Adjunct to diet and exercise to improve glycemic control in adults with T2DM ▪ Dapagliflozin is indicated: – To reduce the risk of hospitalization for HF in adults with T2DM and established CVD or multiple CV risk factors – To reduce the risk of CV death and hospitalization for HF in adults with heart failure with reduced ejection fraction (HFrEF) – To reduce the risk of sustained eGFR decline, ESRD, CV death, and hospitalization for HF in adults with CKD at risk of progression

Hypoglycemics, SGLT2

FDA-Approved Indications

Drug	Manufacturer	Indications
empagliflozin (Jardiance®)[6]	Boehringer Ingelheim	▪ Adjunct to diet and exercise to improve glycemic control in adults and pediatric patients ≥ 10 years of age with T2DM ▪ To reduce the risk of CV death in adults with T2DM and established CVD ▪ To reduce the risk of CV death plus hospitalizations for HF in adults with HFrEF
empagliflozin/ metformin (Synjardy®)[7]	Boehringer Ingelheim	▪ Adjunct to diet and exercise to improve glycemic control in adults and pediatric patients ≥ 10 years of age with T2DM ▪ Empagliflozin is indicated: – To reduce the risk of CV death in adults with T2DM and established CVD – To reduce the risk of CV death and hospitalization for HF in adults with HF

Hypoglycemics, SGLT2

Drug	Manufacturer	Indications
empagliflozin/ metformin ER (Synjardy® XR)[8]	Boehringer Ingelheim	▪ Adjunct to diet and exercise to improve glycemic control in adults with T2DM ▪ Empagliflozin is indicated: – To reduce the risk of CV death in adults with T2DM and established CVD ▪ To reduce the risk of CV death and hospitalization for HF in adults with HF
ertugliflozin (Steglatro®)[9]	Merck, Sharp & Dohme	▪ Adjunct to diet and exercise to improve glycemic control in adults with T2DM
ertugliflozin/ metformin (Segluromet®)[10]	Merck, Sharp & Dohme	▪ Adjunct to diet and exercise to improve glycemic control in adults with T2DM
sotagliflozin (Inpefa™)[11]	Lexicon	▪ To reduce the risk of CV death, hospitalization for HF, and urgent HF visits in adults with HF or T2DM, CKD, and other CV risk factors

Hypoglycemics, SGLT2

- SGLT2 inhibitors are effective in reducing HbA1c, postprandial glucose, and fasting plasma glucose, as well as reducing systolic blood pressure and weight
- The American Diabetes Association (ADA) prefers medications with proven CV and renal benefit in patients with CV and/or renal disease, respectively
- In patients with ASCVD, the addition of empagliflozin (Class A recommendation), liraglutide (Class A recommendation), or canagliflozin (Class C recommendation) is preferred
- In patients with heart failure (HF) or chronic kidney disease (CKD), empagliflozin, canagliflozin, or dapagliflozin is preferred

Hypoglycemics, SGLT2

- 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
- The 2023 American Association of Clinical Endocrinologists (AACE) guidelines include the use of SGLT2 inhibitors as an alternative to metformin for monotherapy and as an appropriate add-on to metformin in dual therapy and triple therapy

Hypoglycemics, SGLT2

- AACE 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
- patients with CKD should be prescribed an SGLT2 inhibitor or GLP-1RA
- 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

Hypoglycemics, SGLT2

- AACE recognizes that empagliflozin and canagliflozin are associated with significantly reduced cardiac mortality, hospitalization for heart failure, as well as secondary renal endpoints
- Additionally, dapagliflozin demonstrated reduced all-cause mortality and the composite of CV death and HF hospitalization; however, it did not significantly lower the combined risk of CV death and nonfatal MI and stroke

Hypoglycemics, SGLT2

- The Kidney Disease Improving Global Outcomes (KDIGO) 2022 guidelines on managing diabetes in CKD recommend first-line treatment with an SGLT2 inhibitor in most patients with an eGFR ≥ 20 mL/min/1.73 m2 (until dialysis or transplant)
- In 2020, the American College of Cardiology (ACC) published an expert consensus decision pathway for CV risk reduction in patients with T2DM
- They identify opportunities to initiate an SGLT2 inhibitor or GLP-1RA with demonstrated CV or renal benefit in patients with T2DM

Hypoglycemics, SGLT2

- A medication from either class may be initiated in any patient with T2DM and ASCVD at the time of diagnosis of T2DM or ASCVD or any time after diagnosis, including at hospital discharge for ASCVD
- An agent from either class can also be started in patients with T2DM without established ASCVD but who are at high risk of ASCVD
- In addition, initiation of an SGLT2 inhibitor with demonstrated CV or renal benefit is recommended in patients with HF and/or diabetic kidney disease; a GLP-1RA is an alternative in patients with eGFR < 30 ml/min/1.73 m^2

Hypoglycemics, SGLT2

- In July 2023, AHA/ACC published guidelines for diagnosis and management for chronic coronary disease (CCD)
- They recommend SGLT2 inhibitors and GLP-1RAs in select patients with CCD, including groups without diabetes
- In September 2015, the FDA issued a safety communication regarding decreased bone mineral density and increased risk of bone fracture associated with canagliflozin use

Hypoglycemics, SGLT2

Guideline Update:

- American College of Physicians (ACP) published guidelines on newer pharmacologic treatments in adults with T2DM, including SGLT2 inhibitors, GLP-1 receptor agonists, GLP-1 agonist/GIP agonists, DPP-4 inhibitors, and long-acting insulins
- Key recommendations include:
  - (1) Adding SGLT2i or GLP-1RA to metformin and lifestyle modifications in those with inadequate glycemic control - use an SGLT-2 inhibitor to reduce the risk for all-cause mortality, MACE, progression of CKD, and hospitalization due to CHF & use a GLP-1RA to reduce the risk for all-cause mortality, MACE, and stroke
  - (2) Do not add DPP-4i to metformin and lifestyle modifications in patients with inadequate glycemic control to reduce morbidity and all-cause mortality
- They also state that sulfonylureas and long-acting insulins are inferior to SGLT-2 inhibitors and GLP-1 agonists in reducing all-cause mortality and morbidity but may still have some limited value for glycemic control

Hypoglycemics, SGLT2

Product Update:

- Indication for Xigduo XR (dapagliflozin/metformin) for use as an adjunct to diet & exercise to improve glycemic control in patients with T2DM has been expanded to include pediatric patients ≥ 10 years of age
- Xigduo was previously only approved for use in adults for this indication
- Recommended starting dosage for this indication for both adults & pediatric patients should be individualized according to patient's current regimen
- Patients not already taking dapagliflozin should start with 5 mg once daily
- Dosage should be adjusted based on tolerability & effectiveness up to a max daily dose of 10 mg dapagliflozin & 2,000 mg metformin

Hypoglycemics, SGLT2

Product Update:

- Indication for Farxiga (dapagliflozin) for use as an adjunct to diet & exercise to improve glycemic control in patients with T2DM has been expanded to include pediatric patients ≥ 10 years of age
- Farxiga was previously only approved for use in adults for this indication
- Recommended dosage for this indication for both adults & pediatric patients is 5 mg orally once daily initially
- Dosage can be increased to 10 mg orally once daily for additional glycemic control

Immune Globulins

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HEALTH CARE COST
CONTAINMENT SYSTEM

Immune Globulins

Drug	Manufacturer	Indications
Intravenous		
Asceniv™[1]	ADMA Biologics	▪ Primary humoral immunodeficiency
Bivigam®[2]	ADMA Biologics	▪ Primary humoral immunodeficiency
Flebogamma® DIF 5% and 10%[3,4]	Grifols	▪ Primary (inherited) immunodeficiency ▪ Chronic primary immune thrombocytopenia (10% only)
Gammagard® S/D[5]	Baxalta	▪ Primary humoral immunodeficiency ▪ Prevention of bacterial infections in hypogammaglobulinemia and/or recurrent bacterial infections associated with B-cell chronic lymphocytic leukemia ▪ Chronic idiopathic thrombocytopenic purpura ▪ Prevention of coronary artery aneurysms associated with Kawasaki syndrome
Gammaplex® 5% and 10%[6,7]	Bio Products Laboratory	▪ Primary humoral immunodeficiency ▪ Chronic immune thrombocytopenic purpura
Octagam® 5% and 10%[8,9]	Octapharma	▪ Primary humoral immunodeficiency (5% only) ▪ Chronic immune thrombocytopenic purpura (10% only) ▪ Dermatomyositis (10% only)
Panzyga®[10]	Octapharma/ Pfizer	▪ Primary humoral immunodeficiency ▪ Chronic immune thrombocytopenia ▪ Chronic inflammatory demyelinating polyneuropathy
Privigen®[11]	CSL Behring	▪ Primary humoral immunodeficiency ▪ Chronic immune thrombocytopenic purpura ▪ Chronic inflammatory demyelinating polyneuropathy (Limitation of use: maintenance therapy has not been studied > 6 months)

Immune Globulins

Intravenous or Subcutaneous		
Gammagard® Liquid[12]	Baxalta	▪ Primary humoral immunodeficiency ▪ Multifocal motor neuropathy
Gammaked™[13]	Kedrion Biopharma*	▪ Primary humoral immunodeficiency ▪ Idiopathic thrombocytopenic purpura (IV use only) ▪ Chronic inflammatory demyelinating polyneuropathy (IV use only)
Gamunex®-C[14]	Grifols	▪ Primary humoral immunodeficiency ▪ Idiopathic thrombocytopenic purpura (IV use only) ▪ Chronic inflammatory demyelinating polyneuropathy (IV use only)
Subcutaneous		
Cutaquig®[15]	Octapharma/ Pfizer	▪ Primary humoral immunodeficiency
Cuvitru®[16]	Shire/Takeda	▪ Primary humoral immunodeficiency
Hizentra®[17]	CSL Behring	▪ Primary immune deficiency ▪ Maintenance therapy in patients with chronic inflammatory demyelinating polyneuropathy
immune globulin 10%/recombinant human hyaluronidase (HyQvia®)[18]	Baxalta	▪ Primary immune deficiency†
Xembify®[19]	Grifols	▪ Primary humoral immunodeficiency

Immune Globulins

The following table outlines the various phenotypic categorizations of PIDD as offered by the American Academy of Allergy, Asthma, and Immunology (AAAAI)

		IgG			
		Quantity/Quality			
		Absent/Absent	Low/Low	Normal/Low	Low/Normal
B cell	Absent	**Category I** ▪ Agamma-globulinemia ▪ SCID			
	Present		**Category II** ▪ Hyper IgM ▪ CVID	**Category III** ▪ Specific Ab Deficiency ▪ NEMO deficiency	**Category IV** ▪ Transient hypogamma-globulinemia of infancy
			▪ NEMO deficiency	▪ Subclass deficiency with specific antibody defect	▪ Primary hypogamma-globulinemia

Ab = antibody, CVID = common variable immunodeficiency, NEMO = NF-kappa B Essential Modulator, SCID = severe combined immunodeficiency

Immune Globulins

- Exogenous immune globulin product has also been FDA approved for use in multifocal motor neuropathy (MMN), chronic inflammatory demyelinating polyneuropathy (CIDP), idiopathic thrombocytopenic purpura (ITP), Kawasaki disease, and B-cell chronic lymphocytic leukemia
- Therapeutic immune globulin is prepared from pooled plasma obtained from healthy donors at plasma donation centers in the US
- These products are purified to contain 95% to 99% IgG with trace amounts of IgA and IgM
- Each product has validated their production methods to ensure low risk of transmission of viruses

Immune Globulins

- Preparation for each product differs in purification, including production methods related to fractionation, exchange chromatography, and filtration
- The AAAAI and the Clinical Immunology Society both recommend product selection to be relied heavily on patient-specific characteristics
- The subcutaneous route is as efficacious as the intravenous route for the treatment of primary immunodeficiencies
- All the products in the class have similar efficacy and safety profiles
- Due to limited supply, the use of immune globulin products should be reserved for approved indications or conditions where the benefit has been clearly established and is consistent with clinical guidelines

Immune Globulins

Product Update:

- FDA has approved new indication for Hyqvia (immune globulin infusion) for treatment of chronic inflammatory demyelinating polyneuropathy (CIDP) as maintenance therapy to prevent relapse of neuromuscular disability and impairment in adults
    - Already indicated for primary immunodeficiency (PI) in adults and pediatric patients ≥ 2 years of age
- For patients switching from IGIV, starting dose and dosing frequency is the same as the patient's previous IGIV treatment
- Product is administered by an HCP, caregiver, or self-administered by the pt after appropriate training
    - Carries a black box warning for thrombosis

Immune Globulins

Product Update:

- FDA approved Gammagard (immune globulin infusion (human), 10%) for improving neuromuscular disability and impairment in adults with Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)
- Already indicated for adults with multifocal motor neuropathy and pediatric patients ≥ 2 years of age for primary humoral immunodeficiency (PI)
- Limitations of use for CIDP include that (1) safety and effectiveness has not been studied in immunoglobulin-naïve patients with CIDP and (2) maintenance therapy in CIDP has not been evaluated beyond 6 months
- Recommended dosage for CIDP is an induction dose is 2 g/kg in divided doses over 2 to 5 consecutive days, followed by maintenance infusions
- Maintenance dose is 1 g/kg in divided doses over 1 to 4 consecutive days, every 3 weeks
- Gammagard is administered IV by an HCP for CIDP

Immune Globulins

Product Update:

- FDA approved Yimmugo (immune globulin intravenous, human-dira) for treatment of primary humoral immunodeficiency (PI) in patients ≥ 2 years of age
- Dosage is 300 to 800 mg/kg (3-8 mL/kg) every 3 to 4 weeks
- Approved as 10% liquid for IV administration
- Carries a black box warning for thrombosis
- The most common adverse reactions were headache, upper respiratory tract infections, fatigue, nausea and increased blood pressure

Immune Globulins

Product Update:

- FDA has approved the following dosage changes for Xembify (immune globulin subcutaneous, human-klhw):
  - (1) Addition of a biweekly dosing option for Primary Humoral Immunodeficiency (PI) in patients ≥ 2 years of age switching from either an IV or SC immune globulin
  - (2) Addition of loading & maintenance dosing for treatment-naïve PI patients ≥ 2 years of age
  - (3) An increase to 35 mL/hour/infusion site for max SC infusion rate for patients with PI who are ≥ 10 years of age

Oncology, Oral - Hematologic

ARIZONA HEALTH CARE COST CONTAINMENT SYSTEM

Oncology, Oral - Hematologic

FDA-Approved Indications

Drug	Manufacturer	FDA-Approved Indications
acalabrutinib (Calquence®)[1,2]	AstraZeneca	▪ Treatment of adults with mantle cell lymphoma (MCL) treated with ≥ 1 prior therapy* ▪ Treatment of adults with chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL)
asciminib (Scemblix®)[3]	Novartis	▪ Treatment of adult patients with chronic phase (CP) Philadelphia chromosome-positive (Ph+) chronic myeloid leukemia (CML) previously treated with ≥ 2 tyrosine kinase inhibitors* ▪ Treatment of adult patients with Ph+ CML in CP with the T315I mutation
azacitidine (Onureg®)[4]	Celgene/BMS	▪ Continued treatment of adult patients with acute myeloid leukemia who achieved first complete remission (CR) or complete remission with incomplete blood count recovery (CRi) following intensive induction chemotherapy and are not able to complete intensive curative therapy
bosutinib (Bosulif®)[5]	Pfizer	▪ Treatment of adults newly-diagnosed chronic phase (CP) Ph+ chronic myeloid leukemia (CML) ▪ Treatment of chronic, accelerated, or blast phase Ph+ CML with resistance or intolerance to prior therapy
busulfan (Myleran®)[6]	Aspen/Prasco LA	▪ Palliative treatment of chronic myelogenous (myeloid, myelocytic, granulocytic) leukemia†
chlorambucil (Leukeran®)[7]	Aspen/Prasco LA	▪ Treatment of chronic lymphatic (lymphocytic) leukemia, malignant lymphomas, including lymphosarcoma, giant follicular lymphoma, and Hodgkin's disease; chlorambucil is not curative in any of these disorders but may produce clinically useful palliation

Oncology, Oral - Hematologic

FDA-Approved Indications

dasatinib (Sprycel®)[8]	Bristol-Meyers Squibb	▪ Treatment of adults with chronic, accelerated, or myeloid or lymphoid blast phase Ph+ CML with resistance or intolerance to prior therapy including imatinib (Gleevec) ▪ Treatment of adults with Ph+ acute lymphoblastic leukemia (ALL) with resistance or intolerance to prior therapy ▪ Newly diagnosed adult patients with Ph+ CML in chronic phase ▪ Treatment of pediatric patients with Ph+ CML in chronic phase ▪ Treatment of pediatric patients with newly diagnosed Ph+ ALL in combination with chemotherapy
decitabine/ cedazuridine (Inqovi®)[9]	Taiho Oncology	▪ Treatment of adults with myelodysplastic syndromes (MDS), including previously treated and untreated, de novo and secondary MDS with the following French-American-British subtypes (refractory anemia, refractory anemia with ringed sideroblasts, refractory anemia with excess blasts, and chronic myelomonocytic leukemia [CMML]) and intermediate-1, intermediate-2, and high-risk International Prognostic Scoring System group
duvelisib (Copiktra®)[10]	Verastem	▪ Relapsed or refractory chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL) after ≥ 2 prior therapies‡
enasidenib (Idhifa®)[11]	Celgene/BMS	▪ Relapsed or refractory acute myeloid leukemia (AML) with an isocitrate dehydrogenase-2 (IDH2) mutation, as determined with an FDA-approved test§

Oncology, Oral - Hematologic

FDA-Approved Indications (continued)

Drug	Manufacturer	FDA-Approved Indications
fedratinib (Inrebic®)[12]	Celgene/BMS	▪ Intermediate-2 or high-risk primary or secondary post-polycythemia vera or post-essential thrombocythemia myelofibrosis (MF)
gilteritinib (Xospata®)[13]	Astellas	▪ Relapsed or refractory adults with AML with a FLT3 mutation, as detected by an FDA-approved test§
glasdegib (Daurismo™)[14]	Pfizer	▪ In combination with low-dose cytarabine, for the treatment of newly diagnosed AML in adult patients who are ≥ 75 years old or who have comorbidities that preclude use of intensive induction chemotherapy
hydroxyurea (Hydrea®)[15]	generic, Bristol-Myers Squibb	▪ Resistant CML ▪ Locally advanced squamous cell carcinomas of the head and neck (excluding lip), in combination with concurrent chemoradiation¶
ibrutinib (Imbruvica®)[16]	Pharmacyclics	▪ Mantle cell lymphoma (MCL) in patients who have received ≥ 1 prior therapy* ▪ CLL/ SLL ▪ CLL/ SLL with 17p deletion ▪ Waldenström's macroglobulinemia ▪ Marginal zone lymphoma (MZL) requiring systemic therapy and patient has had prior anti-CD20-based therapy* ▪ Chronic graft versus host disease (cGVHD) after failure of ≥ 1 line of systemic therapy in adults and pediatric patients ≥ 1 year of age
idelalisib (Zydelig®)[17]	Gilead	▪ Relapsed CLL, in combination with rituximab, in patients for whom rituximab alone would be considered appropriate therapy due to other comorbidities ‖,**

Oncology, Oral - Hematologic

Product Updates:

- nilotinib HCl (February 2024)
  - First generic for Tasigna, by Apotex

- March 2024
  - Alvogen has announced that it will discontinue manufacture of generic melphalan 2 mg tablets due to low sales volume
  - Brand product Alkeran from Apopharma remains on the market

Ophthalmics, Anti-inflammatory/ Immunomodulators

ARIZONA HEALTH CARE COST CONTAINMENT SYSTEM

Ophthalmics, Anti-Inflammatory/Immunomodulators

FDA-Approved Indications

Drug	Manufacturer	Indication
cyclosporine emulsion (Restasis®, Restasis Multidose™)[1,2]	Allergan; generic (Restasis only)	Increase tear production in patients whose tear production is presumed to be suppressed due to ocular inflammation associated with keratoconjunctivitis sicca
cyclosporine emulsion (Verkazia®)[3*]	Eyevance/Harrow	Treatment of vernal keratoconjunctivitis (VKC) in adults and children ≥ 4 years of age
cyclosporine solution (Cequa®)[4*]	Sun	Increase tear production in patients with keratoconjunctivitis sicca (dry eye)
cyclosporine solution (Vevye®)[5]	Harrow	Treatment of signs and symptoms of dry eye disease (DED)
lifitegrast (Xiidra®)[6]	Novartis/ Bausch & Lomb	Treatment of signs and symptoms of DED in adults
loteprednol (Eysuvis®)[7*]	Kala/Alcon	Short-term (up to 14 days) treatment of DED signs and symptoms
perfluorohexyloctane solution (Miebo™)[8]	Bausch & Lomb	Treatment of signs and symptoms of DED
varenicline nasal spray (Tyrvaya®)[9*]	Oyster Point	Treatment of the signs and symptoms of DED in adults

Ophthalmics, Anti-Inflammatory/Immunomodulators

- Dry eye disease (DES)/ Keratoconjunctivitis sicca (KCS) affects approximately 10% to 30% of the US population
- Occurs more commonly in patients over 50 years of age and in postmenopausal women
- According to the 2018 Preferred Practice Parameter on dry eye syndrome and the 2022 Cornea/External Disease Summary Benchmark from the American Academy of Ophthalmology (AAO), artificial tear substitutes are recommended for mild DES

Ophthalmics, Anti-Inflammatory/Immunomodulators

- Recommended measures for moderate dry eyes include use of anti-inflammatory agents, such as topical cyclosporine, lifitegrast, topical corticosteroids, or systemic omega-3 fatty acids supplements, along with artificial tears
- For severe dry eye, in addition to the above-mentioned treatments, systemic cholinergics, systemic anti-inflammatories, mucolytic agents, autologous serum tears, contact lenses, permanent punctal occlusion, and tarsorrhaphy are recommended
- No clinical trials have been published comparing any of the agents in this class, but all have demonstrated efficacy against vehicle

Otic Antibiotics

ARIZONA
HEALTH CARE COST
CONTAINMENT SYSTEM

Otic Antibiotics

FDA-Approved Indications

Drug Name	Manufacturer	Indication(s)
ciprofloxacin (Cetraxal®)[1]	generic, Wraser	▪ Acute otitis externa due to susceptible isolates of *Pseudomonas aeruginosa* or *Staphylococcus aureus* in pediatrics (age 1 year and older) and adults
ciprofloxacin/dexamethasone (Ciprodex® Otic)[2]	Alcon	▪ Acute otitis media in pediatric patients (age 6 months and older) with tympanostomy tubes ▪ Acute otitis externa in pediatric (age 6 months and older), adult, and elderly patients
ciprofloxacin/fluocinolone acetonide (Otovel®)[3]	Arbor	▪ Acute otitis media in pediatric patients (age 6 months and older) with tympanostomy tubes due to *S. aureus, Streptococcus pneumoniae, Haemophilus influenzae, Moraxella catarrhalis,* and *P. aeruginosa*
ciprofloxacin/hydrocortisone (Cipro HC® Otic)[4]	Alcon	▪ Acute otitis externa in adult and pediatric patients (1 year and older) due to *P. aeruginosa, S. aureus,* and *Proteus mirabilis*
neomycin sulfate/colistin sulfate/ thonzonium bromide/ hydrocortisone (Coly-mycin® S)[5]	Endo	▪ Treatment of superficial bacterial infections of the external auditory canal in adult and pediatric patients (1 year and older) ▪ Treatment of infections of mastoidectomy and fenestration cavities in adult and pediatric patients (1 year and older)
neomycin sulfate/polymyxin B/ hydrocortisone[6]	generic	▪ Treatment of superficial bacterial infections of the external auditory canal in adults and pediatric patients (2 years and older)
ofloxacin[7]	generic	▪ Otitis externa in adults and pediatric patients (6 months and older) due to *Escherichia coli, P. aeruginosa*, and *S. aureus* ▪ Chronic suppurative otitis media in patients 12 years and older with perforated tympanic membranes due to *P. mirabilis, P. aeruginosa,* and *S. aureus* ▪ Acute otitis media in pediatric patients (1 year and older) with tympanostomy tubes due to *H. influenzae, M. catarrhalis, P. aeruginosa, S. aureus,* and *S. pneumoniae*

Otic Antibiotics

- The American Academy of Otolaryngology – Head and Neck Surgery Foundation (AAO-HNSF) guidelines for the management of acute otitis externa (AOE) in patients over 2 years of age recommend topical preparations for initial therapy of diffuse, uncomplicated AOE
- A topical aminoglycoside combined with a second antibiotic and a topical steroid, such as the combination of neomycin, polymyxin B, and hydrocortisone is commonly prescribed to treat AOE
- While the addition of a corticosteroid may be of benefit in reducing inflammation, some consider its use unnecessary

Otic Antibiotics

- For acute otitis media, consensus guidelines recommend systemic antibiotics, usually amoxicillin, as first line therapy
- Otic antibiotics provide an alternative to other topical antibiotics in the treatment of acute otitis media in children with tympanostomy tubes
- For chronic suppurative otitis media (CSOM), aminoglycosides or fluoroquinolones can be used
- Aminoglycosides are not recommended to be used if the tympanic membrane is perforated
- Fluoroquinolones are not associated with ototoxicity, and ofloxacin is considered safe in cases of a perforated tympanic membrane

Pulmonary Arterial Hypertension Agents

ARIZONA HEALTH CARE COST CONTAINMENT SYSTEM

Pulmonary Arterial Hypertension

Drug	Manufacturer	Indication(s)
Oral Agents		
ambrisentan (Letairis®)[1]	generic, Gilead	Treatment of pulmonary arterial hypertension (PAH) (World Health Organization [WHO] Group I) to improve exercise ability and delay clinical worsening In combination with tadalafil to reduce the risks of disease progression and hospitalization for worsening PAH, and to improve exercise ability
bosentan (Tracleer®)[2]	generic, Actelion	Treatment of PAH (WHO Group I) in patients with WHO Class II to IV symptoms, to improve exercise ability and decrease clinical worsening Treatment of idiopathic or congenital PAH to improve pulmonary vascular resistance (PVR) in pediatric patients aged ≥ 3 years which is expected to result in an improvement in exercise ability
macitentan (Opsumit®)[3]	Actelion	Treatment of PAH (WHO Group I) to reduce the risks of disease progression and hospitalization for PAH
riociguat (Adempas®)[4]	Bayer	Persistent/recurrent chronic thromboembolic pulmonary hypertension (CTEPH) (WHO Group IV) after surgical treatment or inoperable CTEPH to improve exercise capacity and WHO functional class PAH (WHO Group I) to improve exercise capacity, improve WHO functional class, and to delay clinical worsening
selexipag (Uptravi®)[5]	Actelion	Treatment of PAH (WHO Group I) to delay disease progression and reduce the risk of hospitalization for PAH
sildenafil (Liqrev®)[6]	CMP	Treatment of PAH (WHO Group I) to improve exercise ability and delay clinical worsening in adults
sildenafil (Revatio®)[7]	generic, Pfizer/Viatris	Treatment of PAH (WHO Group I) to improve exercise ability and delay clinical worsening in adults Treatment of PAH (WHO Group I) to improve exercise ability in patients 1 to 17 years of age, and to improve pulmonary hemodynamics thought to underly improvements in exercise in pediatric patients too young to perform standard exercise testing
tadalafil (Adcirca®)[8]	generic, Eli Lilly	Treatment of PAH (WHO Group I) to improve exercise ability
tadaladil (Tadliq®)[9]	CMP	Treatment of PAH (WHO Group I) to improve exercise ability
treprostinil (Orenitram®)[10]	United Therapeutics	Treatment of PAH (WHO Group I) to delay disease progression and to improve exercise capacity

Pulmonary Arterial Hypertension

Drug	Manufacturer	Indication(s)
Inhalation Agents		
iloprost (Ventavis®)[11]	Actelion	Treatment of PAH (WHO Group I) to improve a composite endpoint consisting of exercise tolerance, symptoms (New York Heart Association [NYHA] Class), and lack of deterioration
treprostinil (Tyvaso®, Tyvaso DPI®)[12,13]	United Therapeutics	Treatment of PAH (WHO Group I) to increase exercise ability Treatment of pulmonary hypertension associated with interstitial lung disease (PH-ILD; WHO Group 3) to improve exercise ability

Pulmonary Arterial Hypertension

- The prevalence varies substantially depending on the type, etiology, and underlying condition; estimated to be ~15 per million people
- Pulmonary hypertension (PH) is characterized by an increase in pulmonary arterial pressure and secondary right ventricular failure. This is defined as a resting mean pulmonary arterial pressure (mPAP) ≥ 20 mm Hg
- Symptoms include dyspnea, dizziness, syncope, fatigue, edema (peripheral), angina, palpitations, and other symptoms, all of which are exacerbated by exertion
- PH does not have a cure and, if left untreated, PH is a life-threatening disease with poor prognosis
- Management of PH should be limited to specialized centers where clinicians are experienced in the evaluation and treatment of patients with PH
- Although the number of approved therapies for PAH has grown in the past years, the prognosis is still poor, with a 3-year mortality rate estimated at 21%

Pulmonary Arterial Hypertension

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

Pulmonary Arterial Hypertension

- In treatment-naïve patients with WHO FC II or WHO FC III without rapid disease progression or poor prognosis, initial combination therapy with ambrisentan and tadalafil is suggested
- Monotherapy with ambrisentan, bosentan, sildenafil, macitentan, tadalafil, or riociguat is considered an alternative in patients who are unwilling to take or cannot tolerate combination therapy
- For treatment-naïve patients with WHO FC IV, initial therapy with a parenteral prostanoid agent is recommended
- If the patient cannot comply with parenteral administration, an inhaled prostanoid in combination with an oral endothelin receptor antagonist (ERA) or an oral phosphodiesterase type-5 (PDE-5) inhibitor are alternatives

Pulmonary Arterial Hypertension

- If symptoms remain during treatment with an oral ERA or PDE-5 inhibitor, addition of an inhaled prostanoid is suggested
- In patients with WHO FC III and continued disease progression while on oral mono- or combination therapy, addition of a parenteral or inhaled prostanoid may be considered
- In patients with WHO FC III or IV and an inadequate response to initial therapy with mono- or combination therapy, a second or third class of PAH agents should be added

Pulmonary Arterial Hypertension

- The European Society of Cardiology (ESC) and the European Respiratory Society (ERS), 2022
  - Guidelines for the diagnosis and treatment of pulmonary hypertension includes selexipag (Uptravi) and oral treprostinil (Orenitram)
  - In patients with idiopathic heritable, or drug-associated PAH, negative for vasoreactivity, without cardiopulmonary comorbidities and at low or intermediate risk of death, Selexipag may be added to ERA and PDE-5 inhibitor therapy (Class 2a, Level B)
  - Sequential drug combination therapy to reduce the risk of morbidity/mortality events includes, the addition of selexipag to ERAs and/or PDE-5 inhibitors, and the addition of oral treprostinil to ERA, PDE-5 inhibitor, or riociguat monotherapy (both Class 1, Level B)

Pulmonary Arterial Hypertension Agents

Product Updates:

- FDA approved Opsynvi, a combination of macitentan, an endothelin receptor antagonist (ERA), and tadalafil, a phosphodiesterase 5 (PDE5) inhibitor, for chronic treatment of pulmonary arterial hypertension (PAH, WHO Group I) in adults in WHO functional class (FC) II-III
- Approved as film-coated tablets containing macitentan 10 mg/tadalafil 20 mg and macitentan 10 mg and tadalafil 40 mg
- Dosing is one 10 mg/20 mg or 10 mg/40 mg tablet taken orally once daily
- Boxed warning for embryo-fetal toxicity
    - For all female patients, available only through a REMS program

Pulmonary Arterial Hypertension Agents

Product Updates:

- FDA approved Winrevair (sotatercept-csrk)) , an activin signaling inhibitor indicated for the treatment of adults with pulmonary arterial hypertension (PAH, WHO Group 1) to increase exercise capacity, improve WHO functional class and reduce the risk of clinical worsening events
- Approved as 45 mg and 60 mg lyophilized cake or powder in SDVs
- A weight-based dose is administered SC once every 3 weeks
  - Starting dose is 0.3 mg/kg, with target dose of 0.7 mg/kg
- May be administered by patient or caregiver with proper training
- Warnings include Embryo-Fetal Toxicity, impaired fertility, severe thrombocytopenia, and erythrocytosis

Pulmonary Arterial Hypertension Agents

Product Updates:

- May 2024:
  - Actelion/Philips Respironics has announced discontinuation of the Iloprost (Ventavis) solution in the strengths of 10 ug/mL and 20 ug/mL

Thrombopoiesis Stimulating Agents

Thrombopoiesis Stimulating Agents

FDA-Approved Indications

Drug	Manufacturer	Indication(s)
avatrombopag (Doptelet®)[1]	Akarx	Treatment of thrombocytopenia in adults with chronic immune thrombocytopenia (ITP) who have had an insufficient response to a previous treatment Treatment of thrombocytopenia in adult patients with chronic liver disease (CLD) who are scheduled to undergo a procedure ▪ Avatrombopag should *not* be used in an attempt to normalize platelet counts in patients with CLD
eltrombopag choline (Alvaiz™)[2]	Teva	Treatment of thrombocytopenia in adult and pediatric patients ≥ 6 years of age with persistent or chronic ITP who have had an insufficient response to corticosteroids, immunoglobulins, or splenectomy ▪ Eltrombopag should only be used in patients with ITP whose degree of thrombocytopenia and clinical condition increase the risk for bleeding Treatment of thrombocytopenia in adults with chronic hepatitis C virus (HCV) to allow the initiation and maintenance of interferon-based therapy ▪ Eltrombopag should be used only in patients with chronic HCV whose degree of thrombocytopenia prevents the initiation of interferon-based therapy or limits the ability to maintain interferon-based therapy ▪ Safety and efficacy have not been established in combination with direct acting antiviral agents used without interferon for treatment of chronic HCV infection Treatment of adults with severe aplastic anemia who have had an insufficient response to immunosuppressive therapy Eltrombopag is *not* indicated for the treatment of myelodysplastic syndrome (MDS)

Thrombopoiesis Stimulating Agents

FDA-Approved Indications

Drug	Manufacturer	Indication(s)
eltrombopag olamine (Promacta®)[3]	Novartis	Treatment of thrombocytopenia in adult and pediatric patients ≥ 1 year of age with persistent or chronic ITP who have had an insufficient response to corticosteroids, immunoglobulins, or splenectomy ▪ Eltrombopag should only be used in patients with ITP whose degree of thrombocytopenia and clinical condition increase the risk for bleeding ▪ Eltrombopag should *not* be used in an attempt to normalize platelet counts Treatment of thrombocytopenia in patients with chronic HCV to allow the initiation and maintenance of interferon-based therapy ▪ Eltrombopag should be used only in patients with chronic HCV whose degree of thrombocytopenia prevents the initiation of interferon-based therapy or limits the ability to maintain interferon-based therapy ▪ Safety and efficacy have not been established in combination with direct acting antiviral agents approved for treatment of chronic HCV infection ▪ Eltrombopag should *not* be used in an attempt to normalize platelet counts In combination with standard immunosuppressive therapy for first-line treatment of adult and pediatric patients ≥ 2 years of age with severe aplastic anemia Treatment of patients with severe aplastic anemia who have had an insufficient response to immunosuppressive therapy Eltrombopag is *not* indicated for the treatment of MDS

Thrombopoiesis Stimulating Agents

FDA-Approved Indications (continued)

Drug	Manufacturer	Indication(s)
fostamatinib disodium hexahydrate (Tavalisse®)[4]	Rigel	Treatment of thrombocytopenia in adult patients with chronic ITP who have had an insufficient response to a previous treatment
lusutrombopag (Mulpleta®)[5]	Shionogi	Treatment of thrombocytopenia in adult patients with CLD who are scheduled to undergo a procedure Lusutrombopag should *not* be used in attempt to normalize platelet counts in patients with CLD
romiplostim (Nplate®)[6]	Amgen	Treatment of pediatric patients ≥ 1 year of age with ITP for ≥ 6 months who have had an insufficient response to corticosteroids, immune globulins, or splenectomy Treatment of adults with ITP who have had an insufficient response to corticosteroids, immunoglobulins, or splenectomy To increase survival in adults and in pediatric patients (including term neonates) acutely exposed to myelosuppressive doses of radiation (Hematopoietic Syndrome of Acute Radiation Syndrome [HSARS]) ▪ Romiplostim is *not* indicated to treat thrombocytopenia due to MDS or any cause of thrombocytopenia other than ITP ▪ Romiplostim should only be used in patients with ITP whose degree of thrombocytopenia and clinical condition increases their risk for bleeding ▪ Romiplostim should *not* be used in an attempt to normalize platelet counts

Thrombopoiesis Stimulating Agents

- Thrombocytopenia occurs in 78% of patients with chronic liver disease (CLD) with cirrhosis or fibrosis, and approximately 6% of CLD patients without cirrhosis
- In 2019, the international consensus report on primary ITP provided a review of updated therapies for the management of ITP in children and adults
- Per the consensus, treatment decisions should be individualized depending on the extent of bleeding, platelet count, patient age, presence of fatigue, assessment of risk factors for bleeding, patient preference, and access to care
- Corticosteroids continue to be first-line therapy for the treatment of ITP in adults

Thrombopoiesis Stimulating Agents

- Subsequent treatments with strong evidence include rituximab, the thrombopoietin receptor agonists (TPO-RAs) eltrombopag (Promacta), avatrombopag (Doptelet), and romiplostim (Nplate), as well as fostamatinib (Tavalisse)
- Subsequent therapies with less robust evidence include azathioprine, cyclophosphamide, cyclosporine, danazol, dapsone, mycophenolate mofetil, and vinca alkaloids

Thrombopoiesis Stimulating Agents

- The 2019 American Society of Hematology (ASH) evidence-based practice guidelines for the management of ITP recommends observation or corticosteroids based on platelet count
- Treatment decisions should consider the severity of thrombocytopenia, comorbid conditions, use of antiplatelet or anticoagulant drugs, upcoming procedures, and patient age
- For adults with ITP for ≥ 3 months who are corticosteroid-dependent or unresponsive to steroids, treatment with eltrombopag or romiplostim is suggested

Thrombopoiesis Stimulating Agents

- Either IVIG or anti-D may be used as a first-line therapy if corticosteroids are contraindicated
- Thrombopoietin receptor agonists may be considered for patients at risk for bleeding who have failed at least 1 other therapy and who relapse after splenectomy or have a contraindication to splenectomy
- Thrombopoietin receptor agonists may also be considered in patients at risk for bleeding who have not had a splenectomy and who have failed corticosteroids or IVIG

Thrombopoiesis Stimulating Agents

- Pharmacotherapy for aplastic anemia includes immunosuppressive agents, hematopoietic growth factors, and fludarabine
- Promacta is also indicated to treat first-line and refractory severe aplastic anemia, including in pediatric patients
- Monotherapy with hematopoietic growth factors is not recommended for newly diagnosed patients
- In newly diagnosed children with non-life-threatening mucosal bleeding and/or decreased health-related quality of life (HRQoL), prednisone is suggested rather than IVIG or anti-D
- If these patients are unresponsive to first-line treatment, TPO-RAs are suggested

Ulcerative Colitis

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Ulcerative Colitis

FDA-Approved Indications

Drug	Manufacturer	Indication(s)	
		Treatment	Maintenance
Oral Prodrug Forms			
balsalazide (Colazal®)[1]	generic, Salix	Mildly to moderately active ulcerative colitis (UC) in patients ≥ 5 years	--
olsalazine (Dipentum®)[2]	Meda/Mylan	--	Maintenance of remission of UC in patients intolerant of sulfasalazine
sulfasalazine (Azulfidine®, Azulfidine EN-tabs®)[3,4]	generic*, Pharmacia/ Pfizer	Mildly to moderately active UC Adjunctive therapy in severe UC	Maintenance of remission of UC
		Other: Enteric-coated tablets are indicated in patients with UC who cannot take uncoated sulfasalazine tablets because of gastrointestinal (GI) intolerance Treatment of rheumatoid arthritis that has not responded adequately to salicylates or other nonsteroidal anti-inflammatory agents (NSAIDs) Treatment of pediatric patients with polyarticular juvenile rheumatoid arthritis who have not responded adequately to salicylates or other NSAIDs	

Ulcerative Colitis

Drug	Manufacturer	Indication(s)	
		Treatment	Maintenance
Oral Delayed-Release Forms			
mesalamine delayed-release tablets (Asacol® HD)[5]†	Zydus, Allergan	Moderately active UC	--
mesalamine delayed-release capsules (Delzicol®)[6]‡§	generic, Allergan	Mildly to moderately active UC in patients ≥ 5 years	Maintenance of remission of UC in adults
mesalamine MMX delayed-release tablets (Lialda®)[7]	generic, Shire US	Mildly to moderately active UC in pediatric patients ≥ 24 kg and adults	Maintenance of remission of mildly to moderately active UC in adults
mesalamine extended-release capsules (Pentasa®)[8]	Sun, Shire US	Mildly to moderately active UC	--
mesalamine extended-release capsules (Apriso®)[9]	generic, Salix	--	Maintenance of remission of UC in adults

Ulcerative Colitis

FDA-Approved Indications (continued)

Drug	Manufacturer	Indication(s)	
		Treatment	Maintenance
Rectal Forms			
budesonide rectal foam (Uceris®)[11]	generic, Salix	Mildly to moderately active UC extending up to 40 cm from the anal verge	--
mesalamine enemas (Rowasa®)[12]	generic, Meda/Mylan	Mildly to moderately active distal UC, proctosigmoiditis, or proctitis	--
mesalamine enemas sulfite-free (sfRowasa®)[13]	generic, Meda/Mylan	Mildly to moderately active distal UC, proctosigmoiditis, or proctitis	--
mesalamine suppositories (Canasa®)[14]	generic, Allergan	Mildly to moderately active ulcerative proctitis	--
Oral Corticosteroids			
budesonide extended-release tablets (Uceris®)[15]	generic, Santarus	Mildly to moderately active UC	--

Ulcerative Colitis Agents

- Ulcerative colitis (UC) is a chronic inflammatory disease primarily affecting the colon and rectum
- It is characterized by superficial infiltration of the bowel wall by inflammatory white cells, resulting in multiple mucosal ulcerations and crypt abscesses
- Aminosalicylates remain first-line treatment options for mild to moderate active UC
- The rectal mesalamine products achieve high luminal concentrations of the active component, 5-aminosalicylic acid (5-ASA, mesalamine), while minimizing adverse events from systemic absorption
- Second-line therapy with a course of oral or rectal steroids, such as budesonide (Uceris), is indicated for induction therapy in patients with mild to moderate disease who do not respond to oral and rectal mesalamine agents or in patients with moderate to severe disease
- In patients with severe or refractory UC symptoms, oral corticosteroids are indicated

Ulcerative Colitis Agents

- The 2013 American Academy of Family Physicians (AAFP) guidelines for the diagnosis and treatment of UC recommend 5-ASA (mesalamine) via suppository or enema as first-line for patients with proctitis or proctosigmoiditis, respectively
- Patients unable to tolerate rectally administered 5-ASA therapy may try oral preparations, although response times and remission rates may not be as favorable
- Oral 5-ASA is effective in patients with active mild to moderate UC extending from the proximal to the sigmoid colon
- A 2022 Rapid Evidence Review from AAFP states mesalamine being considered more potent than sulfasalazine
- Budesonide (Uceris), adalimumab, golimumab, vedolizumab, ustekinumab, and tofacitinib were not FDA-approved to treat UC at the time these guidelines were developed

Ulcerative Colitis Agents

- The 2019 American College of Gastroenterology (ACG) clinical guidelines state treatment selection for UC should be based not only on inflammatory activity but also on disease prognosis
- In general, mildly active proctitis and distal UC are treated with rectal 5-ASA
- Oral 5-ASA agents are used, if needed, as add-on for distal UC or to treat extensive disease
- In patients with mildly to moderately active UC who are intolerant or non-responsive to 5-ASA, oral budesonide is recommended to induce remission
- Moderately active UC should be treated with budesonide
- With the exception of corticosteroids, the medication used to induce remission should be continued as maintenance therapy

Ulcerative Colitis Agents

- The American Gastroenterological Association (AGA) developed 2019 practice guidelines for the treatment of mild to moderate UC
- They recommend standard-dose mesalamine or diazo-bonded 5-ASA (balsalazide and olsalazine) for induction and maintenance treatment in patients with extensive mild to moderate UC
- High-dose oral mesalamine combined with rectal 5-ASA may be required for patients with suboptimal response to standard-dose therapy, or in those with moderate or extensive disease
- Oral prednisone or budesonide MMX may be added in those refractory to optimized oral and rectal 5-ASA

Ulcerative Colitis Agents

- The AGA developed 2020 practice guidelines for moderate to severe UC
- First line treatments include infliximab (Remicade®, biosimilars), adalimumab (Humira®, biosimilars), golimumab (Simponi®), vedolizumab (Entyvio®), tofacitinib (Xeljanz®, Xeljanz® XR), or ustekinumab (Stelara®)
- Long-term management of patients with moderate to severe disease can include biologic agents, tofacitinib, or immunomodulators (e.g., azathioprine, methotrexate)
- With the exception of corticosteroids or cyclosporine, if the agent selected for inducing remission is effective, it is usually continued as maintenance therapy

New Drug Reviews

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New Drugs

1. Yorvipath – palopegteriparatide
2. Hympavzi - marstacimab-hncq
3. Livdelzi – seladelpar
4. Aqneursa – levacetylleucine
5. Miplyffa – arimoclomol
6. Ebglyss - lebrikizumab-lbkz
7. Voranigo – vorasidenib

All New Drug are non-preferred

All CMS covered outpatient drugs not listed on the AHCCCS drug list may be eligible through the prior authorization process based on medical necessity

Yorvipath (palopegteriparatide)

- FDA approved palopegteriparatide (Yorvipath), a parathyroid hormone analog (PTH(1-34)), for the treatment of hypoparathyroidism in adults
- Limitations of use include:
  - (1) Not studied for acute post-surgical hypoparathyroidism
  - (2) Titration scheme only evaluated in adults who first achieved an albumin-corrected serum calcium of ≥ 7.8 mg/dL using calcium and active vitamin D treatment
- Approved as single-patient-use prefilled pens containing 168 mcg/0.56 mL, 294 mcg/0.98 mL, and 420 mcg/1.4 mL
- Recommended starting dose is 18 mcg SC once daily and is titrated in 3 mcg increments or decrements with the goal of maintaining serum calcium within the normal range without the need for active vitamin D (e.g., calcitriol) or therapeutic calcium doses (elemental calcium >600 mg/day)
  - Maximum dosage is 30 mcg once daily
  - If adequate response is not achieved with 30 mcg dose, consider adding or restarting calcium and/or active vitamin D therapy and/or seek other treatment options
- Warnings include potential risk of osteosarcoma, orthostatic hypotension, and digoxin toxicity
- Adverse reactions occurring in ≥5% of patients: injection site reactions, vasodilatory signs and symptoms, headache, diarrhea, back pain, hypercalcemia, and oropharyngeal pain

Yorvipath (palopegteriparatide)

- The effectiveness and safety of Yorvipath in adults with hypoparathyroidism were evaluated in a 26-week, randomized, double-blind, placebo-controlled, phase 3 study (Study 1 [NCT04701203]).
- Study 1 was conducted in 82 subjects with hypoparathyroidism
  - Prior to randomization, all subjects underwent an approximate 4-week screening period in which calcium and active vitamin D supplements were adjusted to achieve an albumin-corrected serum calcium concentration between 7.8 and 10.6 mg/dL, a magnesium concentration ≥1.3 mg/dL and below the upper limit of the reference range, and a 25(OH) vitamin D concentration between 20 to 80 ng/mL
  - During the double-blind period, subjects were randomized to either Yorvipath (N = 61) or placebo (N= 21), at a starting dose of 18 mcg/day, co-administered with conventional therapy (calcium and active vitamin D)
  - Randomization was stratified by etiology of hypoparathyroidism (postsurgical vs. all other causes)
  - Study drug and conventional therapy were subsequently titrated according to the albumin-corrected serum calcium levels

Yorvipath (palopegteriparatide)

- Composite primary efficacy outcome of the PaTHway trial was the proportion of participants at week 26 who achieved albumin-adjusted serum calcium in the normal range (8.3–10.6 mg/dL [2.07–2.64 mmol/L]), independence from active vitamin D, and independence from therapeutic doses of elemental calcium (>600 mg/d) with no increase in the prescribed study drug over the 4 weeks before week 26
- Independence from active vitamin D was defined as a daily standing dose equal to zero on all days and use of any PRN active vitamin D on no more than 7 days during the 4 weeks before the week 26 visit
- In the YORVIPATH group, 68.9% (42/61) of subjects met the efficacy endpoint at Week 26 compared with 4.8% (1/21) of subjects in the placebo group
- The treatment difference was 64.2% (95% confidence interval: 49.5%, 78.8%)

Hympavzi (marstacimab-hncq)

- FDA approved marstacimab-hncq (Hympavzi) for routine prophylaxis to prevent or reduce the frequency of bleeding episodes in adults & peds ≥ 12 years of age with hemophilia A (congenital factor VIII deficiency) without factor VIII inhibitors, or hemophilia B (congenital factor IX deficiency) without factor IX inhibitors
- Product will be available as a 150 mg/mL single-dose PFS & single-dose prefilled pen for injection
- Recommended dosage is 300 mg (two 150 mg injections) SC as a loading dose, then 150 mg SC given one week after the loading dose & weekly thereafter
    - Adjustment to 300 mg SC weekly can be considered for pts weighing ≥ 50 kg when control of bleeding events is deemed inadequate
- Factor VIII & factor IX products can be used for breakthrough bleeds; additional doses of Hympavzi should not be used for breakthrough bleeding
- Hympavzi is the first & only anti-tissue factor pathway inhibitor (anti-TFPI) to be approved in the US for hemophilia A & B, and is the first hemophilia tx in the US to be administered via prefilled autoinjector pen once weekly
- Warnings include thromboembolic events and embryo-fetal toxicity

Hympavzi (marstacimab-hncq)

- The efficacy of Hympavzi was established in 116 adult and pediatric patients (aged 12 years and older and ≥35 kg) with severe hemophilia A without FVIII inhibitors or severe hemophilia B without FIX inhibitors enrolled in the BASIS study (NCT03938792), an open-label, multi-center, two-phase study
  - Severe hemophilia is defined as factor activity less than 1%
  - Patients with a history of coronary artery disease, venous or arterial thrombosis or ischemic disease were excluded from the study
- Following screening, patients entered a 6-month observation phase and were enrolled to two cohorts based on the factor replacement treatment they were receiving prior to study entry: on-demand or routine prophylaxis
- Patients who completed the observation phase were to receive 12 months of Hympavzi
- Of the 116 patients who received Hympavzi, 33 patients were in the on-demand treatment cohort and 83 were in the prophylactic treatment with FVIII or FIX cohort during the observation phase
- Patients who completed the 12-month BASIS study were eligible to enroll in an open-label extension study (NCT05145127)

Hympavzi (marstacimab-hncq)

- Patients received an initial 300 mg loading dose of Hympavzi followed by maintenance doses of 150 mg of Hympavzi once weekly for 12 months
- Dose escalation to 300 mg of Hympavzi once weekly was permitted after 6 months of treatment in patients weighing ≥50 kg and experiencing ≥2 breakthrough bleeds
- The efficacy of Hympavzi for each cohort was based upon the ABR of treated bleeds during treatment with Hympavzi compared to ABR during the observational phase
  - Other objectives of the study included evaluation of Hympavzi prophylaxis on the incidences of spontaneous bleeds, joint bleeds, target joint bleeds and total bleeds
- Mean (95% CI) ABR for treated bleeds was reduced for OD (91.6% [88.1-94.1%]) and RP (35.2% [5.6-55.6%]) participants over the 12-month ATP and Hympavzi demonstrated superiority vs OD ($P<0.001$) and non-inferiority and superiority vs RP ($P=0.0376$) therapy
- Hympavzi was also associated with significant reductions in ABR across all breakthrough bleed categories vs OD, and numerical reductions vs RP (non-inferiority)
- The ABR reductions observed with Hympavzi during ATP were consistent across hemophilia types and age groups for OD and were generally consistent across hemophilia types and age groups for RP, with all point estimates for a difference <2.5 (non-inferiority margin for the ABR of treated bleeds)

Livdelzi (seladelpar)

- FDA approved seladelpar (Livdelzi), a peroxisome proliferator-activated receptor (PPAR)-delta agonist, for treatment of primary biliary cholangitis (PBC) in combination with ursodeoxycholic acid (UDCA) in adults with an inadequate response to UDCA, or as monotherapy in patients unable to tolerate UDCA
- Approved under Accelerated Approval based on a reduction of alkaline phosphatase (ALP)
- Approved as 10 mg capsules
- Recommended dosage is 10 mg orally once daily with or without food
- Most common adverse reactions are headache, abdominal pain, nausea, abdominal distension, and dizziness
- Warnings include fractures, liver test abnormalities, and biliary obstruction

Aqneursa (levacetylleucine)

- FDA approved Aqneursa, a modified amino acid, for treatment of neurological manifestations of Niemann-Pick disease type C (NPC) in adults and pediatric patients weighing ≥ 15 kg
- Approved as 1 gram granules for oral suspension in a unit-dose packet
- Recommended dosage is based on the patient's actual body weight
  - Administered orally up to 3 times daily
  - Dose is 1 gram in the morning and evening for pt weighing 15 kg to < 25 kg, 1 g three times a day for patients weighing 25 kg to < 35 kg, and 2 g in morning plus 1 g in afternoon and evening for patient weighing ≥ 35 kg
- Warnings include embryo-fetal toxicity
- Most common adverse reactions are abdominal pain, dysphagia, upper respiratory tract infections, and vomiting

Miplyffa (arimoclomo)

- FDA has approved arimoclomo (Miplyffa) for use in combo with miglustat for treatment of neurological manifestations of Niemann-Pick disease type C (NPC) in adult and pediatric patients ≥ 2 years of age
- Supplied as oral capsules in the strengths of 47 mg, 62 mg, 93 mg, and 124 mg
- Recommended dosage is based on actual body weight
  - 8 kg to 15 kg: 47 mg three times a day
  - > 15 kg to 30 kg: 62 mg three times a day
  - > 30 kg to 55 kg: 93 mg three times a day
  - > 55 kg: 124 mg three times a day)
- Most common adverse reactions (≥15%) are: Upper respiratory tract infection, diarrhea, and decreased weight
- Warnings include embryo-fetal toxicity

Ebglyss (lebrikizumab-lbkz)

- FDA has approved lebrikizumab-lbkz (Ebglyss), an IL-13 antagonist indicated for treatment of adult and pediatric patients ≥ 12 years of age who weigh ≥ 40 kg with moderate-to-severe atopic dermatitis whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable (can be used with or without topical corticosteroids; topical calcineurin inhibitors can be used but reserved for sensitive areas only)
- Will be supplied in 250 mg/2 mL single-dose prefilled pen and prefilled syringe with needle shield
- 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
- Administered SC into the abdomen, thigh, or back of upper arm (by a caregiver or HCP)
- Most common (≥1%) adverse reactions are conjunctivitis, injection site reactions, and herpes zoster

Voranigo (vorasidenib)

- The FDA has approved isocitrate dehydrogenase-1 (IDH1) and isocitrate dehydrogenase-2 (IDH2) inhibitor, vorasidenib (Voranigo), for adult and pediatric patients ≥ 12 years of age with Grade 2 astrocytoma or oligodendroglioma with a susceptible IDH1 or IDH2 mutation, following surgery including biopsy, sub-total resection, or gross total resection
- Supplied as 10 mg and 40 mg oral tablets
- Recommended dosage in adults is 40 mg orally once daily
- Pediatric dosing is based on body weight
  - ≥ 40 kg: 40 mg orally once daily
  - <40 kg: 20 mg orally once daily
- Warnings include embryo-fetal toxicity and hepatotoxicity
- Most common adverse reactions are fatigue, headache, diarrhea, nausea, and seizure

Break and Executive Session

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Public Therapeutic Class Votes

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Biosimilar Update

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Biosimilar Update

- The AGA developed 2020 practice guidelines for moderate to severe UC
- First line treatments include infliximab (Remicade®, biosimilars), adalimumab (Humira®, biosimilars), golimumab (Simponi®), vedolizumab (Entyvio®), tofacitinib (Xeljanz®, Xeljanz® XR), or ustekinumab (Stelara®)
- Long-term management of patients with moderate to severe disease can include biologic agents, tofacitinib, or immunomodulators (e.g., azathioprine, methotrexate)
- With the exception of corticosteroids or cyclosporine, if the agent selected for inducing remission is effective, it is usually continued as maintenance therapy

Future Meeting Dates:

May 20, 2025
October 22, 2025
January 13, 2026

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