





AHCCCS Pharmacy and Therapeutics Committee

January 19, 2022

AHCCCS
Arizona Health Care Cost Containment System

Welcome and Introductions

- Suzi Berman, RPh, AHCCCS Pharmacy Director
  - October 18, 2021 - P&T Minutes Review and Vote
  - All submitted written testimony will be posted on the AHCCCS website under Pharmacy/Pharmacy & Therapeutics Committee

Magellan Class Reviews

Classes for Review: Non-Supplemental Rebate Class Review

- Androgenic Agents
- Antidepressants, Other
- Antidepressants, SSRIs
- Antivirals, Topical
- Bone Resorption Suppression and Related Agents

Magellan Class Reviews

Classes for Review: Non-Supplemental Rebate Class Review

- Bronchodilators, Beta Agonists
- Colony Stimulating Factors
- Enzyme Replacement, Gaucher Disease
- Erythropoiesis Stimulating Proteins
- Hypoglycemics, Alpha Glucosidase Inhibitors

Magellan Class Reviews

Classes for Review: Non-Supplemental Rebate Class Review

- Hypoglycemics, Metformins
- Hypoglycemics, SGLT2s
- Immune Globulins
- Oncology, Oral – Hematologic
- Ophthalmics, Anti-inflammatory/Immunomodulators

Magellan Class Reviews

Classes for Review: Non-Supplemental Rebate Class Review

- Otic Antibiotics
- PAH Agents, Oral and Inhaled
- Thrombopoiesis Stimulating Agents
- Ulcerative Colitis




Magellan Drug Class Reviews

Sarah Martinez, Pharm.D.

Androgenic Agents

Androgenic Agents

Class Overview:

- testosterone 1 %, 1.62% gel – Androgel, testosterone gel
- testosterone gel – Fortesta, Vogelxo, testosterone gel
- testosterone 1% gel – Testim, testosterone gel
- testosterone nasal gel – Natesto
- testosterone solution
- testosterone transdermal - Androderm

Androgenic Agents

- Male hypogonadism is caused by insufficient production of testosterone and characterized by low serum concentrations
- Hypogonadism may present as testosterone deficiency, infertility, or both
- Transdermal delivery of testosterone is appealing to some patients as it is convenient to use and eliminates frequent office visits often required by injectable testosterone
- The 2002 treatment guidelines for hypogonadism published by the American Association of Clinical Endocrinologists (AACE) advise that testosterone replacement therapy can enable the patient to function in a more normal manner and decrease the risk of future associated problems

Androgenic Agents

- The 2018 Endocrine Society (ES) treatment guidelines for hypogonadism recommend a diagnosis of hypogonadism be made only if the patient has symptoms of testosterone deficiency, with clear and consistently low serum testosterone (T) levels
- Serum testosterone, hematocrit, and prostate cancer risk should be monitored during the first year of treatment
- The ES provides advantages and disadvantages of each formulation, but no preference for any testosterone replacement product is provided
- Choice of formulation should be based on patient preference and drug pharmacokinetics, adverse effect profile, treatment burden, and cost

Androgenic Agents

- 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

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
- In response, AACE/American College of Endocrinology (ACE) issued a position statement indicating that the correlation of cardiovascular risk may be due to low testosterone serving as a marker of cardiovascular disease rather than testosterone supplementation as a causative factor

Antidepressants, Other

Antidepressants, Other

Drug	Manufacturer	Major Depressive Disorder (MDD)	Generalized Anxiety Disorder (GAD)	Social Anxiety Disorder (SAD)	Panic Disorder	Other Indications
bupropion HBr (Aplenzin®)	Valeant/Bausch	X	--	--	--	--
bupropion HCl ER (Forfivo XL®)	generic*, Almatica	X	--	--	--	--
bupropion HCl ER (Wellbutrin® XL)	generic, Valeant/Bausch	X	--	--	--	prevention of major depressive episodes associated with seasonal affective disorder
bupropion HCl IR	generic	X	--	--	--	--

Antidepressants, Other

Drug	Manufacturer	Major Depressive Disorder (MDD)	Generalized Anxiety Disorder (GAD)	Social Anxiety Disorder (SAD)	Panic Disorder	Other Indications
bupropion HCl SR (Wellbutrin® SR)	generic, GlaxoSmithKline	X	--	--	--	--
desvenlafaxine ER base	Ranbaxy/Sun	X	--	--	--	--
desvenlafaxine succinate ER (Pristiq®)	generic, Wyeth/Pfizer	X	--	--	--	--

Antidepressants, Other

Drug	Manufacturer	Major Depressive Disorder (MDD)	Generalized Anxiety Disorder (GAD)	Social Anxiety Disorder (SAD)	Panic Disorder	Other Indications
duloxetine (Cymbalta®)	generic, Eli Lilly	X	X	--	--	diabetic peripheral neuropathic pain; fibromyalgia; chronic musculoskeletal pain
duloxetine delayed-release (Drizalma Sprinkle™)	Sun	X	X	--	--	diabetic peripheral neuropathic pain; 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	--	--	--	--

‡ Esketamine (Spravato) is a Schedule III controlled substance. The effectiveness of esketamine in preventing suicide or reducing suicidal death has not been demonstrated; its use does not preclude the need for hospitalization, when clinically needed, regardless of patient symptom improvement following an initial dose. Esketamine is not approved as an anesthetic agent; its safety and efficacy as such has not been demonstrated.

Antidepressants, Other

Drug	Manufacturer	Major Depressive Disorder (MDD)	Generalized Anxiety Disorder (GAD)	Social Anxiety Disorder (SAD)	Panic Disorder	Other Indications
isocarboxazid (Marplan®)	Medilink/ Validus	X 2nd line therapy	--	--	--	--
levomilnacipran (Fetzima®)	Allergan/Forest	X	--	--	--	--
mirtazapine tablet and ODT (Remeron®; Remeron SolTab)	generic, Merck/Organon	X	--	--	--	--

Antidepressants, Other

Drug	Manufacturer	Major Depressive Disorder (MDD)	Generalized Anxiety Disorder (GAD)	Social Anxiety Disorder (SAD)	Panic Disorder	Other Indications
nefazodone	Teva	X	--	--	--	--
phenelzine (Nardil®)	generic, Pfizer	X 2nd line therapy	--	--	--	--
selegiline (Emsam®)	Mylan Specialty	X	--	--	--	--
tranylcypromine (Parnate®)	generic, Concordia	X 2nd line therapy	--	--	--	--

Antidepressants, Other

Drug	Manufacturer	Major Depressive Disorder (MDD)	Generalized Anxiety Disorder (GAD)	Social Anxiety Disorder (SAD)	Panic Disorder	Other Indications
trazodone	generic	X	--	--	--	--
venlafaxine	generic	X	--	--	--	--
venlafaxine ER capsule (Effexor XR®)	generic, Wyeth/Pfizer	X	X	X	X	--
venlafaxine ER tablet (Venlafaxine ER)	generic, Trigen	X	--	X	--	--

Antidepressants, Other

Drug	Manufacturer	Major Depressive Disorder (MDD)	Generalized Anxiety Disorder (GAD)	Social Anxiety Disorder (SAD)	Panic Disorder	Other Indications
vilazodone HCl (Viibryd®)	Allergan	X	--	--	--	--
vortioxetine (Trintellix®)	Takeda	X	--	--	--	--

Antidepressants, Other

- In the US, approximately 17.3 million adults, or 7.1% of the adult population, have reported the prevalence of depression in 2017
- Per the 2016 American College of Physicians (ACP) guidelines, treatment with either CBT or second-generation antidepressants for major depressive disorder (MDD) is recommended
- 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
- SSRIs are first-line agents for the treatment of anxiety disorders in children

Antidepressants, Other

- 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
- Esketamine (Spravato) carries a boxed warning for risk of dissociation and sedation after administration as well as abuse and misuse and 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

Antidepressants, Other

- The 2008 WFSBP guidelines recommend SSRIs, SNRIs, and pregabalin as first-line therapies for the treatment of anxiety, obsessive-compulsive, and post-traumatic stress disorders [CBT and other variants of behavior therapy are recommended either alone or in combination with these medications]
- The 2009 American Psychiatric Association (APA) treatment guidelines recommend SSRIs, SNRIs, TCAs, and benzodiazepines as first-line pharmacotherapy for panic disorder
- For Seasonal Affective Disorder, the International Consensus Group on Depression and Anxiety (ICGDA) expert panel guidelines recommend SSRIs as first-line therapy

Antidepressants, Other

- Treatment-resistant depression (TRD) occurs in approximately 20% to 30% of patients with MDD.
- 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 [e.g., multiple drugs or drug plus psychotherapy), augmentation, or other nonpharmacologic therapy (e.g., light therapy, electroconvulsive therapy in select patients]

Antidepressants, Other

- In 2018, the North American Menopause Society and National Network on Depression Centers published consensus guidelines for the treatment of perimenopausal depression
- These note that SSRIs and SNRIs, particularly desvenlafaxine, have been shown to improve menopause-associated symptoms [e.g., vasomotor symptoms, pain, sleep disturbances, night sweats); however, none of the agents in this class are approved for symptoms of menopause]

Antidepressants, Other

Guideline Update:

- The American Academy of Child and Adolescent Psychiatry (AACAP) published a practice guideline on the assessment and treatment of anxiety disorders in children and adolescents in 2020.
- AACAP recommends that SSRIs should be offered to patients 6 to 18 years of age with social anxiety, generalized anxiety, separation anxiety, or panic disorder (1B).
- The combination of CBT and an SSRI could be offered preferentially over either CBT or an SSRI alone in the same population (2C). Data supporting the use of other antidepressants are fewer; however, AACAP states that SNRIs could be offered to patients ≥ 6 years of age with social anxiety, generalized anxiety, separation anxiety, or panic disorder (2C).

Antidepressants, SSRIs

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	--	--	--	--	--	--	--
fluoxetine	generic, Alvogen	X (≥ 8 years)	--	--	X	--	X (≥ 7 years)	--	X	--
fluoxetine (Prozac®)	generic, Dista	X (≥ 8 years)	--	--	X	--	X (≥ 7 years)	--	X	--

Antidepressants, SSRIs

Drug	Mfr	MDD	GAD	SAD	Panic Disorder	PTSD	OCD	PMDD	Bulimia Nervosa	VMS
fluoxetine (Sarafem®)	generic, Actavis/ Allergan	--	--	--	--	--	--	X	--	--
fluoxetine ER	generic	X	--	--	--	--	--	--	--	--
fluvoxamine	generic, ANI	--	--	--	--	--	X (≥ 8 years)	--	--	--
fluvoxamine ER	Dr. Reddy's	--	--	--	--	--	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 (Brisdelle®)	generic, Sebela	--	--	--	--	--	--	--	--	X

Antidepressants, SSRIs

Drug	Mfr	MDD	GAD	SAD	Panic Disorder	PTSD	OCD	PMDD	Bulimia Nervosa	VMS
paroxetine mesylate (Pexeva®)	Sebela	X	X	--	X	--	X	--	--	--
sertraline capsules	Almatica	X	--	--	--	--	X (≥ 6 years)	--	--	--
sertraline tablets, oral solution (Zoloft®)	generic, Pfizer	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
- 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

Antivirals, Topical

Antivirals, Topical

Drug	Manufacturer	Indication
acyclovir cream (Zovirax®)	generic, Valeant	Treatment of recurrent herpes labialis (cold sores) in immunocompetent adults and children 12 years of age and older
acyclovir ointment (Zovirax®)	generic, Valeant	Management of initial genital herpes and in limited non-life-threatening mucocutaneous herpes simplex virus infections in immunocompromised adult patients
acyclovir/ hydrocortisone (Xerese®)	Valeant	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®)	Mylan	Treatment of recurrent herpes labialis (cold sores) in adults and children 12 years of age and older

Antivirals, Topical

- 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.
- Compared to placebo, treatment has reduced lesion healing time by approximately 0.75 to 1.5 days in clinical trials

Antivirals, Topical

- 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

Bronchodilators, Beta Agonist

Bronchodilators, Beta Agonist

Class Overview: Long-Acting Agents

- aformoterol tartrate - (Brovana Solution)
- formoterol fumarate - (Perforomist Solution)
- indacaterol maleate - (Arcapta Neohaler)*
- olodaterol HCl - (Striverdi Respimat)
- salmeterol xinafoate - (Serevent Diskus)

*In March 2020, Sunovion reported to the FDA the discontinuation of indacaterol (Arcapta Neohaler) production. Product may remain available until supply is depleted

Bronchodilators, Beta Agonist

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 Agonist

Class Overview: Oral Agents

- albuterol sulfate - (albuterol ER, syrup & tablet)
- metaproterenol sulfate - (metaproterenol 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 Agonist

- Prevalence and incidence of asthma in the U.S. continues to rise, affecting approximately 7.7% of adults and 8.4% of children (25.2 million Americans). It is estimated that the number of Americans with a COPD diagnosis is approximately 16 million.
- $Beta_2$-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 $beta_2$-agonists (LABAs) as controller medications

Bronchodilators, Beta Agonist

- These agents lead to improvements in symptoms, reducing the need for short-acting beta$_2$-agonists (SABAs) for quick relief by relaxing airway smooth muscle
- 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 Agonist

- 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 Agonist

- 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 Agonist

- 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 Agonist

- The 2021 GINA guidelines offer a control-based management plan which adjusts treatment through a continuous cycle of assessment and review of the patient's response to therapy as it relates to symptom control, future risk of exacerbations, and side effects.
- The GINA 2021 guidelines describe 2 treatment tracks: Track 1 and Track 2. 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.
- The 2021 GOLD guidelines place a great focus on the assessment of inhaler technique and adherence to improve therapeutic outcomes

Bronchodilators, Beta Agonist

- 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, respectively. 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), but 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 Agonist

- 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. Choosing Wisely recommends 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 and state that typically a single agent, such as a low-dose ICS or leukotriene modifier, is sufficient to maintain asthma control

Bronchodilators, Beta Agonist

- 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 Agonist

- 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 Agonist

Stepwise Approach to Asthma Control* from 2021 GINA Guidelines – Controller and Reliever Therapy in Patients ≥ 12 Years Old[42]

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 SABA	--
2	▪ As-needed low dose ICS/formoterol	▪ Low dose maintenance ICS ▪ With 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 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 SABA	▪ Add LAMA or add LTRA 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) ▪ 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 ▪ With as-needed SABA	▪ Add azithromycin (adults) or add LTRA or add low dose oral corticosteroid (considering adverse effects)

HDM SLIT = house dust mite sublingual immunotherapy; ICS = inhaled corticosteroid; IgE = Immunoglobulin E; IL-5 = interleukin-5; LABA = long acting beta$_2$-agonist; LTRA = leukotriene receptor antagonist; SABA = short acting beta$_2$-agonist

Bronchodilators, Beta Agonist

Stepwise Approach to Asthma Control* from 2021 GINA Guidelines – Controller and Reliever Therapy in Patients 6 to 11 Years Old[43]

Step	Preferred Controller	Other Controller Options	Reliever
1	▪ Low dose ICS whenever SABA is taken	▪ Daily low dose ICS	▪ As needed SABA
2	▪ Daily low dose ICS	▪ Daily LTRA or low dose ICS whenever SABA is taken	▪ As needed SABA
3	▪ Low dose ICS/LABA or medium dose ICS, or very low dose ICS/formoterol MART	▪ Low dose ICS + LTRA	▪ As needed SABA (or ICS/formoterol for MART)
4	▪ Medium dose ICS/LABA or low dose ICS/formoterol MART; refer for expert advice	▪ Add tiotropium or LTRA	▪ As needed SABA (or ICS/formoterol for MART)
5	▪ Refer for phenotypic assessment; ± higher dose ICS/LABA or add-on therapy (e.g., anti-IgE [omalizumab])	▪ Add-on anti-IL-5 or add low dose oral corticosteroid (considering adverse effects)	▪ As needed SABA (or ICS/formoterol for MART)

ICS = inhaled corticosteroid; IgE = Immunoglobulin E; IL-5 = interleukin-5; LABA = long acting beta$_2$-agonist; LTRA = leukotriene receptor antagonist; MART = maintenance and reliever therapy; SABA = short acting beta$_2$-agonist

Bronchodilators, Beta Agonist

2021 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 C	Group D

Bone Resorption Suppression and Related Agents

Bone Resorption Suppression and Related Agents

Drug	Manufacturer	Indication(s)
Bisphosphonates		
alendronate (Binosto®)	Mission, Ascend	Treatment and prevention of osteoporosis in postmenopausal women Treatment to increase bone mass in men with osteoporosis
alendronate (Fosamax®)	generic, Merck	Treatment and prevention of osteoporosis in postmenopausal women Treatment to increase bone mass in men with osteoporosis Treatment of glucocorticoid-induced osteoporosis in men and women receiving glucocorticoids in a daily dosage equivalent of 7.5 mg or greater of prednisone and who have low bone mineral density Treatment of Paget's disease of bone in men and women
alendronate/ vitamin D (Fosamax® Plus D)	Merck	Treatment of osteoporosis in postmenopausal women Treatment to increase bone mass in men with osteoporosis

Bone Resorption Suppression and Related Agents

Drug	Manufacturer	Indication(s)
etidronate	generic	Treatment of Paget's disease of bone Prevention and treatment of heterotopic ossification following total hip replacement or spinal cord injury
ibandronate (Boniva®)	generic, Roche	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 or greater of prednisone for chronic diseases Treatment of Paget's disease of bone in men and women

Bone Resorption Suppression and Related Agents

Drug	Manufacturer	Indication(s)
risedronate delayed-release (Atelvia®)	generic, Actavis/ Allergan	Treatment of osteoporosis in postmenopausal women
Others		
abaloparatide (Tymlos®)	Radius Health	Treatment of osteoporosis in postmenopausal women who are at high risk for fractures

Bone Resorption Suppression and Related Agents

Drug	Manufacturer	Indication(s)
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 in men and women at high risk for fracture. Treatment of bone loss in men with prostate cancer on androgen deprivation therapy Treatment of bone loss in women undergoing breast cancer therapy with adjuvant aromatase therapy Treatment to increase bone mass in men diagnosed with osteoporosis and a high fracture risk who have failed or are intolerant to other potential therapies

Bone Resorption Suppression and Related Agents

Drug	Manufacturer	Indication(s)
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 Increase of bone mass in men with primary or hypogonadal osteoporosis who are at high risk for fracture Treatment of men and women with osteoporosis associated with sustained systemic glucocorticoid therapy at high risk for fracture

* Approved via an abbreviated approval pathway under a 505(b)(2) application that relied, in part, on safety and efficacy data for Eli Lilly's teriparatide (Forteo).

Bone Resorption Suppression and Related Agents

Drug	Manufacturer	Indication(s)
teriparatide (Forteo®)	Eli Lilly	Treatment of osteoporosis in postmenopausal women who are at high risk for fractures Increase of bone mass in men with primary or hypogonadal osteoporosis who are at high risk for fractures Treatment of men and women with osteoporosis associated with sustained systemic glucocorticoid therapy at high risk for fracture
Calcitonins		
calcitonin-salmon	generic	Treatment of postmenopausal osteoporosis in females greater than 5 years postmenopause when alternative treatments are not suitable. Fracture reduction efficacy has not been demonstrated

Bone Resorption Suppression and Related Agents

- Approximately 10 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

- According to the American College of Physicians' (ACP) published update in 2017 for the treatment of low bone density and osteoporosis to prevent fractures in men and women, pharmacologic treatment to reduce the risk for hip and vertebral fractures in women with known osteoporosis and treatment should occur for 5 years
- ACP recommends against using menopausal estrogen or estrogen with progesterone or raloxifene for osteoporosis treatment in women
- Regarding therapy in men, the ACP recommends that clinicians offer treatment with bisphosphonates to reduce the risk of vertebral fractures in those with clinical osteoporosis

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
- 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

- The 2020 ES 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, calcitonin, and hormone replacement therapy are only recommended if patients are not appropriate candidates for treatment with bisphosphonates or denosumab

Bone Resorption Suppression and Related Agents

- American Society for Bone and Mineral Research, American Association of Clinical Endocrinologists, Endocrine Society, European Calcified Tissue Society, and National Osteoporosis Foundation issued a joint statement on the management of osteoporosis during COVID-19 pandemic
- Oral bisphosphonate therapy should not be delayed and patients already taking the medication should continue treatment
- BMD exams may need to be delayed and standard pretreatment lab work for IV bisphosphates or denosumab may be skipped if results in prior year were normal

Bone Resorption Suppression and Related Agents

- Alternative methods of delivering parenteral medications for osteoporosis may be considered or temporarily delaying denosumab, teriparatide, abaloparatide, or romosozumab may be considered in patients who are unable to receive prescribed therapy
- Patients may need to temporarily transition to oral bisphosphonates if denosumab dose is delayed by ≥ 1 month or if teriparatide, abaloparatide, or romosozumab dose is delayed by > 2-3 months

Bone Resorption Suppression and Related Agents

Guideline Update:

- 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.

Bone Resorption Suppression and Related Agents

Guideline Update:

- 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
- 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 antiremodeling therapy.

Colony Stimulating Factors

Colony Stimulating Factors

Drug	Manufacturer	Cancer Patients Receiving Myelo-suppressive Chemotherapy	Acute Myeloid Leukemia (AML) Patients Receiving Chemotherapy	Bone Marrow Transplant (BMT)	Peripheral Blood Progenitor Cell Collection and Therapy	Severe Chronic Neutropenia	Hematopoietic Syndrome of Acute Radiation Syndrome
filgrastim (Neupogen®)	Amgen	X	X	X[a]	X	X	X
filgrastim-aafi (Nivestym™)	Pfizer	X	X	X[a]	X	X	--
filgrastim-sndz (Zarxio®)	Sandoz	X	X	X[a]	X	X	--
pegfilgrastim (Neulasta®)	Amgen	X	--	--	--	--	X

[a] In cancer patients receiving BMT to reduce duration of neutropenia and febrile neutropenia

Colony Stimulating Factors

Drug	Manufacturer	Cancer Patients Receiving Myelo-suppressive Chemotherapy	Acute Myeloid Leukemia (AML) Patients Receiving Chemotherapy	Bone Marrow Transplant (BMT)	Peripheral Blood Progenitor Cell Collection and Therapy	Severe Chronic Neutropenia	Hematopoietic Syndrome of Acute Radiation Syndrome
pegfilgrastim-apgf (Nyvepria™)	Pfizer	X	--	--	--	--	--
pegfilgrastim-cbqv (Udenyca™)	Coherus	X	--	--	--	--	--
pegfilgrastim-jmdb (Fulphila™)	Mylan	X	--	--	--	--	--

Colony Stimulating Factors

Drug	Manufacturer	Cancer Patients Receiving Myelo-suppressive Chemotherapy	Acute Myeloid Leukemia (AML) Patients Receiving Chemotherapy	Bone Marrow Transplant (BMT)	Peripheral Blood Progenitor Cell Collection and Therapy	Severe Chronic Neutropenia	Hematopoietic Syndrome of Acute Radiation Syndrome
pegfilgrastim-bmez (Ziextenzo™)	Sandoz	X	--	--	--	--	--
sargramostim (Leukine®)	Sanofi/ Partner	--	X	X[b]	X	--	X
tbo-filgrastim (Granix®)	Cephalon/ Teva	X	--	--	--	--	--

[b] For acceleration of myeloid reconstitution after PBPC/BMT; treatment of delayed neutrophil recovery or graft failure after BMT

Colony Stimulating Factors

- Colony stimulating factors (CSF) are hematopoietic growth factors that have been shown to decrease the likelihood of chemotherapy-induced neutropenic complications and to improve relative chemotherapy dose intensity
- Prophylactic CSF use can reduce the severity, risk, and duration of febrile neutropenia and decrease rates of infection
- Filgrastim (Neupogen), filgrastim-aafi (Nivestym), filgrastim-sndz (Zarxio), pegfilgrastim (Neulasta), pegfilgrastim-apgf (Nyvepria), pegfilgrastim-cbqv (Udenyca), pegfilgrastim-jmdb (Fulphila), pegfilgrastim-bmez (Ziextenzo), and tbo-filgrastim (Granix) are granulocyte colony-stimulating factors (G-CSF). Sargramostim (Leukine) is a granulocyte-macrophage colony stimulating factor (GM-CSF).

Colony Stimulating Factors

- The administration frequency of pegfilgrastim and its biosimilars may be viewed as more favorable since these only require a single SC injection per chemotherapy cycle; whereas filgrastim, filgrastim-aafi (Nivestym), filgrastim-sndz (Zarxio), tbo-filgrastim (Granix), and sargramostim (Leukine) administration requires daily subcutaneous injection
- Several biosimilars to the originator products, filgrastim (filgrastim-aafi and filgrastim-sndz) and pegfilgrastim (pegfilgrastim-cbqv, pegfilgrastim-bmez, pegfilgrastim-apgf, pegfilgrastim-jmdb, and pegfilgrastim-apgf) are now available

Colony Stimulating Factors

- The v2.2021 NCCN practice guidelines for hematologic growth factors indicate there is higher level evidence supporting the use of filgrastim, filgrastim-aafi, filgrastim-sndz, tbo-filgrastim, and pegfilgrastim (category 1) for prophylactic use against febrile neutropenia
- Pegfilgrastim-cbqv and pegfilgrastim-jmdb are rated a category 2A and sargramostim is no longer recommended in this setting. Sargramostim is used for treatment but no longer recommended for prophylaxis.

Colony Stimulating Factors

- The guidelines note that biosimilars are biological products that are highly similar to their FDA-approved originator product with very small, clinically inactive differences but have no difference in efficacy, safety, or purity. However, NCCN states limited data suggest that patients can alternate between the originator product and the biosimilar without any clinically meaningful differences regarding efficacy or safety.

Colony Stimulating Factors

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

Colony Stimulating Factors

Product Update:

- For breast and lung cancer patients, filgrastim, pegfilgrastim, and their biosimilars are associated with an increased risk of Myelodysplastic Syndrome (MDS) and Acute Myeloid Leukemia (AML) when used in conjunction with chemotherapy and/or radiation.
- Patients should be monitored for signs and symptoms of MDS and AML.

Gaucher Disease

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 (≥ 2 years of age) and adults with confirmed type 1 Gaucher disease that results in 1 or more 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 and older: 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 ▪ Mix gently; do not shake

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 (≥ 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

Gaucher Disease

FDA-Approved Indications and Dosages (continued)

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 (Zavesca®)[6]	generic†, 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

* Eliglustat (Cerdelga) limitations of use: CYP2D6 ultra-rapid metabolizers may not achieve adequate concentrations of eliglustat to achieve a therapeutic dose; a specific dosage cannot be recommended for CYP2D6 indeterminate metabolizers.

† Authorized generic is available.

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

Erythropoiesis Stimulating Proteins

Erythropoiesis Stimulating Proteins

Drug	Manufacturer	FDA-Approved Indications
darbepoetin (Aranesp®)	Amgen	▪ Treatment of anemia associated with chronic kidney disease (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 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 red blood cell (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

Erythropoiesis Stimulating Proteins

Drug	Manufacturer	FDA-Approved Indications
luspatercept-aamt (Reblozyl®)	Celgene	▪ Treatment of anemia in adult patients with beta thalassemia who require regular red blood cell (RBC) transfusions ▪ Treatment of anemia failing an erythropoiesis stimulating agent and requiring ≥ 2 RBC units over 8 weeks in adult patients with very low- to intermediate-risk myelodysplastic syndromes 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®)	Roche/Vifor	▪ Treatment of anemia associated with chronic renal failure (CRF) in adult patients on dialysis and adult patients not on dialysis ▪ Treatment of anemia associated with CRF in pediatric patients 5 to 17 years of age on hemodialysis who are converting from another ESA after their hemoglobin level was stabilized with an erythropoiesis stimulating agent (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 in patients receiving cancer chemotherapy – PEG-EPO is not indicated as a substitute for red blood cell (RBC) transfusion in patients who require immediate correction of anemia

Erythropoiesis Stimulating Proteins

Drug	Manufacturer	FDA-Approved Indications
rHuEPO (Epogen®)	Amgen	▪ Treatment of anemia associated with CRF including patients on dialysis and patients not on dialysis to decrease the need for red blood cell (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 m Units/mL ▪ Treatment of anemia in patients with non-myeloid malignancies where anemia is due to the effect of concomitant myelosuppressive chemotherapy and, upon initiation, hemoglobin < 10 g/dL and there is a minimum of 2 additional months of planned chemotherapy ▪ Indicated to reduce the need for allogenic RBC transfusion among patients with perioperative hemoglobin > 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 whom anemia can be managed by transfusion – rHuEPO is not indicated as a substitute for red blood cell (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®)	Amgen (distributed by Janssen)	

Erythropoiesis Stimulating Proteins

Drug	Manufacturer	FDA-Approved Indications
rHuEPO-epbx (Retacrit®)	Pfizer (Hospira)	▪ Treatment of anemia associated with CKD including patients on dialysis and patients not on dialysis to decrease the need for red blood cell (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 hemoglobin > 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

- Anemia affects over 3 million Americans as it is a result of numerous diseases, as well as adverse effects of treatments
- Erythropoietin is a glycoprotein produced in the kidneys that stimulates red blood cell production from bone marrow
- 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 v4.2021 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, which is defined as anemia following the initiation of chemotherapy and continues up to 6 weeks following the end of treatment.

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
- This joint 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

Hypoglycemics, Alpha-Glucosidase Inhibitors

Hypoglycemics, Alpha-Glucosidase Inhibitors

Class Overview:

- acarbos – 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

Hypoglycemics, Metformins

PRODUCT LIST AND 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

Hypoglycemics, Metformins

PRODUCT LIST AND FDA-APPROVED INDICATIONS

Drug	Manufacturer	Indications
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

- Per the 2020 American Diabetes Association (ADA) Standards of Medical Care in Diabetes, metformin is recommended as initial therapy for the treatment of T2DM, along with lifestyle interventions at the time of diagnosis, unless metformin is contraindicated
- The American Association of Clinical Endocrinologists (AACE) and American College of Endocrinology (ACE) clinical practice guidelines recommend metformin as first-line therapy, and as the highest recommended agent among all anti-hyperglycemic medications for monotherapy
- The American College of Physicians' (ACP) revised 2017 guidelines for T2DM recommend metformin as first-line 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, Metformins

Guideline Update:

- Updates in the 2022 Standards of Medical Care in Diabetes to the include:
  - Guidance on first-line therapy determined by co-morbidities.
  - Screening for prediabetes and diabetes beginning at age 35 for all people.
  - Changes to gestational diabetes mellitus (GDM) recommendations regarding when to test and in whom testing should be done.
  - Updated recommendations on technology selection

Hypoglycemics, Metformins

Guideline Update:

- Additional considerations have been added to the recommendation regarding metformin therapy:
- Metformin therapy for prevention of type 2 diabetes should be considered in adults with prediabetes, as typified by the Diabetes Prevention Program, especially those aged 25–59 years with BMI ≥35 kg/m2, higher fasting plasma glucose (e.g., ≥110 mg/dL), and higher A1C (e.g., ≥6.0%), and in women with prior gestational diabetes mellitus.
- Metformin should be continued upon initiation of insulin therapy (unless contraindicated or not tolerated) for ongoing glycemic and metabolic benefits.

Hypoglycemics, Metformins

Guideline Update:

- More discussion of overtreatment was added to the “Pharmacologic Therapy” subsection “Older Adults”, as was the consideration that for those taking metformin long term, monitoring vitamin B12 deficiency should be considered.

Hypoglycemics, SGLT2

Hypoglycemics, SGLT2

Drug	Manufacturer	Indications
canagliflozin (Invokana®)	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 kidney disease, doubling of serum creatinine, cardiovascular (CV) death, and hospitalization for heart failure in adults T2DM and diabetic nephropathy with albuminuria > 300 mg/day
canagliflozin/ metformin (Invokamet®)	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 ▪ Canagliflozin is indicated to reduce the risk of end-stage kidney disease, doubling of serum creatinine, CV death, and hospitalization for heart failure in adults with T2DM and diabetic nephropathy with albuminuria
canagliflozin/ metformin ER (Invokamet® XR)	Janssen	

Hypoglycemics, SGLT2

Drug	Manufacturer	Indications
dapagliflozin (Farxiga®)	AstraZeneca	▪ Adjunct to diet and exercise to improve glycemic control in adults with T2DM ▪ To reduce the risk of hospitalization for heart failure in adults with T2DM and established CVD or multiple CV risk factors ▪ To reduce the risk of CV death and hospitalization for heart failure (HF) in adults with HF (NYHA class II-IV) with reduced ejection fraction ▪ To reduce the risk of sustained eGFR decline, end stage kidney disease (ESKD), CV death, and hospitalization for heart failure (hHF) in adults with chronic kidney disease (CKD) at risk of progression
dapagliflozin/ metformin ER (Xigduo® XR)	AstraZeneca	▪ Adjunct to diet and exercise to improve glycemic control in adults with T2DM ▪ Dapagliflozin is indicated to reduce the risk of hospitalization for heart failure in adults with T2DM and established CVD or multiple CV risk factors.

Hypoglycemics, SGLT2

Drug	Manufacturer	Indications
empagliflozin (Jardiance®)	Boehringer Ingelheim	▪ Adjunct to diet and exercise to improve glycemic control in adults with T2DM ▪ To reduce the risk of cardiovascular death in adults with T2DM and established CVD ▪ To reduce the risk of cardiovascular death and hospitalization for heart failure in adults with heart failure and reduced ejection fraction (HFrEF)
empagliflozin/ metformin (Synjardy®)	Boehringer Ingelheim	▪ Adjunct to diet and exercise to improve glycemic control in adults with T2DM when treatment with both empagliflozin and metformin is appropriate ▪ Empagliflozin is indicated to reduce the risk of cardiovascular death in adults with T2DM and established CVD*
empagliflozin/ metformin ER (Synjardy® XR)	Boehringer Ingelheim	

Hypoglycemics, SGLT2

Drug	Manufacturer	Indications
ertugliflozin (Steglatro™)	Merck, Sharp & Dohme	▪ Adjunct to diet and exercise to improve glycemic control in adults T2DM
ertugliflozin/ metformin (Segluromet™)	Merck, Sharp & Dohme	▪ Adjunct to diet and exercise to improve glycemic control in adults with T2DM

Hypoglycemics, SGLT2

- The 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 American Association of Clinical Endocrinologists (AACE) and American College of Endocrinology (ACE) 2020 diabetes management algorithm and 2015 clinical practice guidelines for developing a diabetes care plan 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/ACE 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
- In the 2020 algorithm, the panel identifies SGLT2 inhibitors as having a neutral effect on bone

Hypoglycemics, SGLT2

- 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.
- 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.

Hypoglycemics, SGLT2

- 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 m2

Hypoglycemics, SGLT2

Product/Guideline Updates:

- FDA approved a new indication for Farxiga (dapagliflozin) to reduce the risk of sustained eGFR decline, end stage kidney disease (ESKD), CV death, and hospitalization for heart failure (hHF) in adults with chronic kidney disease (CKD) at risk of progression.
- Corresponding new limitations of use were also added stating that dapagliflozin is not recommended for use to improve glycemic control in adults with type 2 diabetes mellitus with an eGFR < 45 mL/min/1.73 m2 as it is unlikely to be effective based upon its mechanism of action.

Hypoglycemics, SGLT2

Product/Guideline Updates:

- FDA updated the Steglatro (ertugliflozin) indication to remove the limitation of use for "those who are not adequately controlled on a regimen containing ertugliflozin or metformin, or in patients who are already treated with both ertugliflozin and metformin".
- The package insert was updated to state that use is not recommended in pts with eGFR < 45 mL/min/1.73 m2 (still contraindicated with eGFR < 30 mL/min/1.73 m2); contraindication updated to include hypersensitivity to any excipient.
- Updates were also made to the warnings section regarding ketoacidosis, lower limb amputation, volume depletion, urosepsis and pyelonephritis, necrotizing fasciitis, and vitamin B12 deficiency.

Hypoglycemics, SGLT2

Product/Guideline Updates:

- Jardiance (empagliflozin) is now approved to reduce the risk of cardiovascular death and hospitalization for heart failure in adults with heart failure and reduced ejection fraction (HFrEF).

Hypoglycemics, SGLT2

Product/Guideline Updates:

- Updates in the 2022 Standards of Medical Care in Diabetes include:
  - "Cardiovascular Disease: Treatment" subsection, providing guidance for patients with type 2 diabetes and established ASCVD or multiple risk factors for ASCVD on the use of combined therapy with a SGLT2 inhibitor with demonstrated cardiovascular benefit and a GLP-1 receptor agonist with demonstrated cardiovascular benefit.
  - "Chronic Kidney Disease and Risk Management Recommendation" has been revised to include lower glomular filtration rates and lower urinary albumin as indicators for use of SGLT2 inhibitors to reduce CKD progression and cardiovascular events.

Hypoglycemics, SGLT2

Product/Guideline Updates:

- The USPSTF has issued a final recommendation statement (August 2021) on screening for prediabetes and type 2 diabetes.
- It is recommended to screen for prediabetes and type 2 diabetes in adults aged 35 to 70 years who are overweight or obese, and health care providers should offer or refer patients with prediabetes for preventive interventions (Grade B).

Immune Globulins

Immune Globulins

Drug	Manufacturer	Indications
Intravenous		
Asceniv™	ADMA	Primary humoral immunodeficiency
Bivigam®	Biotest/ADMA	Primary humoral immunodeficiency
Flebogamma® DIF 5% and 10%	Grifols	▪ Primary (inherited) immunodeficiency ▪ Chronic primary immune thrombocytopenia (10% only)
Gammagard® S/D	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%	Bio Products Laboratory	▪ Primary humoral immunodeficiency ▪ Chronic immune thrombocytopenic purpura

Immune Globulins

Drug	Manufacturer	Indications
Octagam® 5% and 10%	Octapharma	▪ Primary humoral immunodeficiency (5% only) ▪ Chronic immune thrombocytopenic purpura (10% only) ▪ Dermatomyositis (10% only)
Panzyga®	Octapharma/ Pfizer	▪ Primary humoral immunodeficiency ▪ Chronic immune thrombocytopenia ▪ Chronic inflammatory demyelinating polyneuropathy
Privigen®	CSL Behring	▪ Primary humoral immunodeficiency ▪ Chronic immune thrombocytopenic purpura ▪ Chronic inflammatory demyelinating polyneuropathy (Limitation of use: maintenance therapy has not been studied > 6 months)
Intravenous or Subcutaneous		
Gammagard® Liquid	Baxalta	▪ Primary humoral immunodeficiency ▪ Multifocal motor neuropathy

Immune Globulins

Drug	Manufacturer	Indications
Gammaked™	Kedrion Biopharm†	▪ Primary humoral immunodeficiency ▪ Idiopathic thrombocytopenic purpura (IV use only) ▪ Chronic inflammatory demyelinating polyneuropathy (IV use only)
Gamunex®-C	Grifols Therapeutics	▪ Primary humoral immunodeficiency ▪ Idiopathic thrombocytopenic purpura (IV use only) ▪ Chronic inflammatory demyelinating polyneuropathy (IV use only)
Subcutaneous		
Cutaquig®	Octapharma/ Pfizer	▪ Primary humoral immunodeficiency
Cuvitru™	Shire/Takeda	▪ Primary humoral immunodeficiency

Immune Globulins

Drug	Manufacturer	Indications
Hizentra®	CSL Behring	▪ Primary immune deficiency ▪ Maintenance therapy in patients with chronic inflammatory demyelinating polyneuropathy
immune globulin 10%/recombinant human hyaluronidase (Hyqvia®)	Baxalta	▪ Primary immune deficiency†
Xembify®	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/Guideline Updates:

- FDA approved expanded indication for Cutaquig to include pediatric patients 2 to 17 years of age for the treatment of primary humoral immunodeficiency

Oncology Oral, Hematologic Cancers

Oncology Oral, Hematologic Cancers

Drug	Manufacturer	FDA-Approved Indications
acalabrutinib (Calquence®)	AstraZeneca	▪ Treatment of adults with mantle cell lymphoma (MCL) treated with ≥ 1 prior therapy ▪ Treatment of adult patients with chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL)
azacitidine (Onureg®)	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®)	Pfizer	▪ Newly diagnosed chronic phase (CP) Ph+ CML ▪ Treatment of chronic, accelerated, or blast phase Ph+ chronic myeloid leukemia (CML) with resistance or intolerance to prior therapy
busulfan (Myleran®)	Aspen/ Prasco LA	▪ Palliative treatment of chronic myelogenous (myeloid, myelocytic, granulocytic) leukemia†

Oncology Oral, Hematologic Cancers

Drug	Manufacturer	FDA-Approved Indications
chlorambucil (Leukeran®)	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
dasatinib (Sprycel®)	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

Oncology Oral, Hematologic Cancers

Drug	Manufacturer	FDA-Approved Indications
decitabine/ cedazuridine (Inqovi®)	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®)	Verastem	▪ Relapsed or refractory chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL) after ≥ 2 prior therapies ▪ Relapsed or refractory follicular lymphoma (FL) after ≥ 2 prior systemic therapies
enasidenib (Idhifa®)	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 Cancers

Drug	Manufacturer	FDA-Approved Indications
fedratinib (Inrebic®)	Celgene	▪ Intermediate-2 or high-risk primary or secondary post-polycythemia vera or post-essential thrombocythemia myelofibrosis (MF)
gilteritinib (Xospata®)	Astellas	▪ Relapsed or refractory adults with AML with a FLT3 mutation, as detected by an FDA-approved test
glasdegib (Daurismo™)	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®)	generic, Bristol-Myers Squibb	▪ Resistant CML ▪ Locally advanced squamous cell carcinomas of the head and neck (excluding lip), in combination with concurrent chemoradiation‖

Oncology Oral, Hematologic Cancers

Drug	Manufacturer	FDA-Approved Indications
ibrutinib (Imbruvica®)	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
idelalisib (Zydelig®)	Gilead	▪ Relapsed chronic CLL in combination with rituximab in patients for whom rituximab alone would be considered appropriate therapy due to other comorbidities¶ ▪ Relapsed follicular B-cell non-Hodgkin's lymphoma in patients who have received ≥ 2 prior systemic therapies*,¶ ▪ Relapsed SLL in patients who have received ≥ 2 prior systemic therapies*,¶

Oncology Oral, Hematologic Cancers

Drug	Manufacturer	FDA-Approved Indications
imatinib (Gleevec®)	generic, Novartis	▪ Newly diagnosed adult and pediatric patients with Ph+ CML in chronic phase ▪ Patients with Ph+ CML in blast crisis, accelerated phase, or chronic phase after failure of interferon-alpha therapy ▪ Adult patients with relapsed or refractory Ph+ ALL ▪ Pediatric patients with newly diagnosed Ph+ ALL in combination with chemotherapy ▪ Adult patients with myelodysplastic/ myeloproliferative diseases associated with platelet-derived growth factor receptor (PDGFR) gene re-arrangements as determined with an FDA-approved test‡ ▪ Adult patients with aggressive systemic mastocytosis without the D816V c-Kit mutation, as determined with an FDA-approved test or with c-Kit mutational status unknown‡ ▪ Adult patients with hypereosinophilic syndrome and/or chronic eosinophilic leukemia who have the FIP1L1-PDGFRα fusion kinase (mutational analysis or FISH demonstration of CHIC2 allele deletion) and for patients with hypereosinophilic syndrome and/or chronic eosinophilic leukemia who are FIP1L1-PDGFRα fusion kinase-negative or unknown ▪ Adult patients with unresectable, recurrent, and/or metastatic dermatofibrosarcoma protuberans (DFSP) ▪ Patients with Kit (CD117)-positive unresectable and/or metastatic malignant gastrointestinal stromal tumors (GIST) ▪ Adjuvant treatment of adult patients following resection of Kit (CD117)-positive GIST

Oncology Oral, Hematologic Cancers

Drug	Manufacturer	FDA-Approved Indications
ivosidenib (Tibsovo®)	Agios	▪ Adult patients with relapsed or refractory AML with a susceptible isocitrate dehydrogenase-1 (IDH1) mutation, as detected by an FDA-approved test‡ ▪ Adult patients with newly diagnosed AML who are ≥ 75 years old or who have comorbidities that preclude the use of intensive induction chemotherapy with a susceptible IDH1 mutation, as detected by an FDA-approved test
ixazomib (Ninlaro®)	Millennium	▪ In combination with lenalidomide and dexamethasone for the treatment of multiple myeloma in patients who have received ≥ 1 prior therapy

Oncology Oral, Hematologic Cancers

Drug	Manufacturer	FDA-Approved Indications
lenalidomide (Revlimid®)	Celgene/BMS	▪ In combination with dexamethasone for the treatment of multiple myeloma ▪ As maintenance therapy for multiple myeloma following autologous hematopoietic stem cell transplantation (auto-HSCT) ▪ Treatment of transfusion-dependent anemia due to low-or intermediate-1-risk myelodysplastic syndromes associated with a deletion of 5q cytogenetic abnormality with or without additional cytogenetic abnormalities ▪ Treatment of mantle cell lymphoma after relapse or disease progression after 2 prior therapies, 1 of which included bortezomib ▪ In combination with a rituximab product for the treatment of previously treated FL ▪ In combination with a rituximab product for the treatment of previously treated MZL
melphalan (Alkeran®)	generic, Apopharma	▪ Palliative treatment of multiple myeloma ▪ Palliation of non-resectable epithelial carcinoma of the ovary

Oncology Oral, Hematologic Cancers

Drug	Manufacturer	FDA-Approved Indications
mercaptopurine (Purixan®),	generic (tablets); Nova (suspension)	▪ ALL as a component of a combination maintenance therapy regimen
midostaurin (Rydapt®)	Novartis	▪ Newly diagnosed AML that is FLT3 mutation-positive as detected by an FDA-approved test‡, in combination with standard cytarabine and daunorubicin induction and cytarabine consolidation** ▪ Aggressive systemic mastocytosis (ASM), systemic mastocytosis with associated hematological neoplasm (SM-AHN), or mast cell leukemia
nilotinib (Tasigna®)	Novartis	▪ Accelerated phase and chronic phase Ph+ CML in adult patients resistant to or intolerant to prior therapy that included imatinib (Gleevec) ▪ Newly diagnosed adult and pediatric patients ≥ 1 year of age with Ph+ CML in chronic phase ▪ Treatment of chronic phase Ph+ CML with resistance or intolerance to prior tyrosine kinase inhibitor (TKI) therapy in pediatric patients ≥ 1 year of age

Oncology Oral, Hematologic Cancers

Drug	Manufacturer	FDA-Approved Indications
panobinostat (Farydak®)	Novartis/ Secura	▪ Treatment of multiple myeloma in combination with bortezomib and dexamethasone in patients who have received ≥ 2 prior regimens, including bortezomib and an immunomodulatory agent
pomalidomide (Pomalyst®)	Celgene/BMS	▪ For use in combination with dexamethasone for patients with multiple myeloma who have received ≥ 2 prior therapies including lenalidomide and a proteasome inhibitor and have demonstrated disease progression on or within 60 days of completion of the last therapy ▪ For the treatment of adults with acquired immunodeficiency syndrome (AIDS)-related Kaposi sarcoma (KS) after failure of highly active antiretroviral therapy (HAART), as well as for the treatment of KS in adults who are human immunodeficiency virus (HIV)-negative

Oncology Oral, Hematologic Cancers

Drug	Manufacturer	FDA-Approved Indications
ponatinib (Iclusig®)	Ariad/Takeda, Millennium	▪ Treatment of adult patients with chronic phase (CP) CML with resistance or intolerance to ≥ 2 prior kinase inhibitors ▪ Treatment of adult patients with T315I-positive chronic myeloid leukemia (CML) (chronic phase, accelerated phase, or blast phase) or T315I-positive Philadelphia chromosome positive acute lymphoblastic leukemia (Ph+ALL) ▪ Treatment of adult patients with chronic phase, accelerated phase, or blast phase chronic myeloid leukemia or Ph+ALL for whom no other TKI is indicated††
procarbazine (Matulane®)	Leadiant	▪ For use in combination with other anticancer drugs for the treatment of stage 3 and stage 4 Hodgkin's disease; used as part of the MOPP regimen (nitrogen mustard, vincristine, procarbazine, prednisone)

Oncology Oral, Hematologic Cancers

Drug	Manufacturer	FDA-Approved Indications
ruxolitinib (Jakafi®)	Incyte	▪ Intermediate or high-risk MF, including primary MF, post-polycythemia vera MF and post-essential thrombocythemia MF ▪ Treatment of polycythemia vera in patients who have had an inadequate response to or are intolerant of hydroxyurea ▪ Treatment of steroid-refractory acute graft versus host disease (GVHD) in adult and pediatric patients ≥ 12 years of age
selinexor (Xpovio™)	Karyopharm	▪ In combination with bortezomib and dexamethasone for the treatment of adults with multiple myeloma who have received ≥ 1 prior therapy ▪ In combination with dexamethasone for the treatment of relapsed or refractory multiple myeloma (RRMM) who have received ≥ 4 prior therapies and whose disease is refractory to ≥ 2 proteasome inhibitors, ≥ 2 immunomodulatory agents, and an anti-CD38 monoclonal antibody ▪ Treatment of adults with relapsed or refractory diffuse large B-cell lymphoma (DLBCL), not otherwise specified, including DLBCL arising from follicular lymphoma, after ≥ 2 lines of systemic therapy

Oncology Oral, Hematologic Cancers

Drug	Manufacturer	FDA-Approved Indications
thalidomide (Thalomid®)	Celgene/BMS	▪ Treatment of newly diagnosed multiple myeloma in combination with dexamethasone ▪ Acute treatment of cutaneous manifestations of moderate to severe erythema nodosum leprosum (ENL)‡‡ ▪ Prevention and suppression of cutaneous manifestations of ENL recurrence as maintenance therapy
thioguanine (Tabloid®)	Aspen/ Prasco LA	▪ For remission induction and remission consolidation of acute nonlymphocytic leukemias§
tretinoin	generic	▪ For remission induction in patients with acute promyelocytic leukemia (APL), FAB classification M3 characterized by the presence of the t(15;17) translocation and/or presence of the PML/RARα gene who are refractory to, have relapsed from, or have a contraindication to anthracycline chemotherapy‖‖

Oncology Oral, Hematologic Cancers

Drug	Manufacturer	FDA-Approved Indications
thalidomide (Thalomid®)	Celgene/BMS	▪ Treatment of newly diagnosed multiple myeloma in combination with dexamethasone ▪ Acute treatment of cutaneous manifestations of moderate to severe erythema nodosum leprosum (ENL)‡‡ ▪ Prevention and suppression of cutaneous manifestations of ENL recurrence as maintenance therapy
umbralisib (Ukoniq™)	TG Therapeutics	▪ Relapsed or refractory MZL who have received ≥ 1 prior anti-CD20-based regimen* ▪ Relapsed or refractory FL who have received ≥ 3 prior lines of systemic therapy*
venetoclax (Venclexta®)	AbbVie	▪ Treatment of CLL or SLL in adult patients ▪ In combination with azacitidine, decitabine, or low-dose cytarabine for the treatment of newly diagnosed AML in adults who are age 75 years or older or who have comorbidities that preclude use of intensive induction chemotherapy*

Oncology Oral, Hematologic Cancers

Drug	Manufacturer	FDA-Approved Indications
vorinostat (Zolinza®)	Merck, Sharp & Dohme	▪ Treatment of cutaneous manifestations of cutaneous T-cell lymphoma (CTCL) in patients who have progressive, persistent, or recurrent disease on or following 2 systemic therapies
zanubrutinib (Brukinsa™)	Beigene	▪ Treatment of adult patients with mantle cell lymphoma (MCL) who have received ≥ 1 prior therapy*

Ophthalmics, Anti-Inflammatory/Immunomodulator

Ophthalmics, Anti-Inflammatory/Immunomodulator

PRODUCT LIST AND FDA-APPROVED INDICATIONS

Drug	Manufacturer	Indication
cyclosporine emulsion (Restasis®, Restasis Multidose®)[1,2]	Allergan	Increase tear production in patients whose tear production is presumed to be suppressed due to ocular inflammation associated with keratoconjunctivitis sicca
cyclosporine solution* (Cequa™)[3]	Sun	Increase tear production in patients with keratoconjunctivitis sicca (dry eye)
lifitegrast (Xiidra®)[4]	Shire/Novartis	Treatment of signs and symptoms of dry eye disease in adults
loteprednol (Eysuvis™)[5]	Kala	Short-term (up to 14 days) treatment of dry eye disease signs and symptoms

* Cequa (cyclosporine) and Eysuvis (loteprednol) were approved under the United States (US) Food and Drug Administration (FDA) 505(b)(2) pathway that allows at least some data submitted for approval to be from studies not conducted by or for the applicant.[6, 7, 8]

Ophthalmics, Anti-Inflammatory/Immunomodulator

- Dry eye disease (DES)/ Keratoconjunctivitis sicca (KCS) affects approximately 10% to 30% of the US population and occurs more commonly in patients over 40 years of age and in postmenopausal women
- According to the 2018 Preferred Practice Parameter on dry eye syndrome and the 2020 Cornea/External Disease Summary Benchmark from the American Academy of Ophthalmology (AAO), artificial tear substitutes are recommended for mild DES

Ophthalmics, Anti-Inflammatory/Immunomodulator

- Recommended measures for moderate dry eyes include use of anti-inflammatory agents, such as topical cyclosporine (Cequa, Restasis, Restasis Multidose), lifitegrast (Xiidra), 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

Otic Antibiotics

PRODUCT LIST AND FDA-APPROVED INDICATIONS

Drug Name	Manufacturer	Indication(s)
ciprofloxacin (Cetraxal®)	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)	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®)	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)	Alcon	▪ Acute otitis externa in adult and pediatric patients (1 year and older) due to *P. aeruginosa, S. aureus,* and *Proteus mirabilis*

Otic Antibiotics

PRODUCT LIST AND FDA-APPROVED INDICATIONS

Drug Name	Manufacturer	Indication(s)
neomycin sulfate/colistin sulfate/ thonzonium bromide/ hydrocortisone (Coly-mycin® S)	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	generic	▪ Treatment of superficial bacterial infections of the external auditory canal in adults and pediatric patients (2 years and older)
ofloxacin	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 the use of corticosteroids 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 (PAH) Agents, Oral and Inhaled

Pulmonary Arterial Hypertension (PAH) Agents, Oral and Inhaled

Drug	Manufacturer	Indication(s)
Oral Agents		
ambrisentan (Letairis®)	generic, Gilead	Treatment of pulmonary arterial hypertension (World Health Organization [WHO] Group I) to improve exercise ability and delay clinical worsening In combination with tadalafil to reduce the risks of disease progression and hospitalization for worsening PAH, and to improve exercise ability
bosentan (Tracleer®)	generic, Actelion	Treatment of pulmonary arterial hypertension (WHO Group I) in patients with WHO Class II to IV symptoms, to improve exercise ability and decrease clinical worsening Treatment of idiopathic or congenital PAH to improve pulmonary vascular resistance (PVR) in pediatric patients aged 3 years and older which is expected to result in an improvement in exercise ability
macitentan (Opsumit®)	Actelion	Treatment of pulmonary arterial hypertension (WHO Group I) to delay disease progression which includes death, initiation of intravenous (IV) or subcutaneous (SC) prostanoids, or clinical worsening; Opsumit also reduced hospitalization for PAH

Pulmonary Arterial Hypertension (PAH) Agents, Oral and Inhaled

Drug	Manufacturer	Indication(s)
riociguat (Adempas®)	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 Pulmonary arterial hypertension (WHO Group I) to improve exercise capacity, improve WHO functional class and to delay clinical worsening
selexipag (Uptravi®)	Actelion	Treatment of pulmonary arterial hypertension (WHO Group I) to delay disease progression and reduce the risk of hospitalization for PAH
sildenafil (Revatio®)	generic, Pfizer	Treatment of pulmonary arterial hypertension (WHO Group I) to improve exercise ability and delay clinical worsening
tadalafil (Adcirca®)	generic, Eli Lilly	Treatment of pulmonary arterial hypertension (WHO Group I) to improve exercise ability

Pulmonary Arterial Hypertension (PAH) Agents, Oral and Inhaled

Drug	Manufacturer	Indication(s)
treprostinil (Orenitram®)	United Therapeutics	Treatment of pulmonary arterial hypertension (WHO Group I) to delay disease progression and to improve exercise capacity
Inhalation Agents		
iloprost (Ventavis®)	Actelion	Treatment of pulmonary arterial hypertension (WHO Group I) to improve a composite endpoint consisting of exercise tolerance, symptoms (NYHA Class), and lack of deterioration
treprostinil (Tyvaso®)	United Therapeutics	Treatment of pulmonary arterial hypertension (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 (PAH) Agents, Oral and Inhaled

- The treatment for pulmonary arterial hypertension (PAH) is complex
- A trial of high dose oral calcium channel blockers (CCB), such as amlodipine, diltiazem, or nifedipine, is recommended in patients with a positive acute vasoreactive test
- Alternative or additional PAH therapy should be initiated if improvement to WHO FC I or II are not seen after the trial of a CCB
- The 2018 updated American College of Chest Physicians (CHEST) guidelines on therapy for pulmonary arterial hypertension in adults provide treatment recommendations based on World Health Organization (WHO) functional class (FC) for patients who are not candidates for, or who have failed, high-dose oral calcium channel blocker (CCB) therapy

Pulmonary Arterial Hypertension (PAH) Agents, Oral and Inhaled

- 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 (PAH) Agents, Oral and Inhaled

- 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 (PAH) Agents, Oral and Inhaled

- The European Society of Cardiology (ESC) and the European Respiratory Society (ERS) 2015 recommendations for the diagnosis and treatment of pulmonary hypertension include Selexipag as an option for monotherapy or in combination with an ERA and/or PDE-5 inhibitor in patients with WHO FC II or III
- ESC/ERS also include oral treprostinil as an option for monotherapy in patients with WHO FC III

Pulmonary Arterial Hypertension (PAH) Agents, Oral and Inhaled

Product/Guideline Updates:

- Tyvaso (treprostinil) is now approved for the treatment of pulmonary hypertension associated with interstitial lung disease (PH-ILD; WHO Group 3) to improve exercise ability.
- It is the only agent in this class approved for this indication

Thrombopoiesis Stimulating Proteins

Thrombopoiesis Stimulating Proteins

Drug	Manufacturer	Indication(s)
avatrombopag (Doptelet®)	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 chronic liver disease (CLD)

Thrombopoiesis Stimulating Proteins

Drug	Manufacturer	Indication(s)
eltrombopag (Promacta®)	Novartis	Treatment of thrombocytopenia in adult and pediatric patients ≥ 1 year of age with persistent or chronic immune thrombocytopenia (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 patients with chronic hepatitis C (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 myelodysplastic syndrome (MDS)

Thrombopoiesis Stimulating Proteins

Drug	Manufacturer	Indication(s)
fostamatinib disodium hexahydrate (Tavalisse™)	Rigel	Treatment of thrombocytopenia in adult patients with chronic immune thrombocytopenia (ITP) who have had an insufficient response to a previous treatment
lusutrombopag (Mulpleta®)	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

Thrombopoiesis Stimulating Proteins

Drug	Manufacturer	Indication(s)
romiplostim (Nplate®)	Amgen	Treatment of pediatric patients ≥ 1 year of age with immune thrombocytopenia (ITP) for ≥ 6 months who have had an insufficient response to corticosteroids, immune globulins, or splenectomy Treatment of adults with chronic immune thrombocytopenia (ITP) who have an insufficient response with 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 myelodysplastic syndrome (MDS) or any cause of thrombocytopenia other than chronic 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 Proteins

- Thrombocytopenia occurs in 64% to 84% 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 Proteins

- 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 Proteins

- The 2019 updated American Society of Hematology (ASH) evidence-based practice guidelines for the management of immune thrombocytopenia 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 the patient's age
- For adults with ITP for ≥ 3 months who are corticosteroid-dependent or unresponsive to steroids, treatment with eltrombopag or romiplostim is suggested (very low certainty)

Thrombopoiesis Stimulating Proteins

- Either IVIG or anti-D may be used as a first-line therapy if corticosteroids are contraindicated (grade 2C)
- 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 (grade 1B)
- 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 (grade 2C)

Thrombopoiesis Stimulating Proteins

- 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 Agents

Ulcerative Colitis Agents

Drug	Manufacturer	Indication(s)	
		Treatment	Maintenance
Oral Prodrug Forms			
balsalazide (Colazal®)	generic, Salix	Mild to moderately active ulcerative colitis (UC) in patients ≥ 5 years	--
olsalazine (Dipentum®)	Meda/Mylan	--	Maintenance of remission of UC in patient's intolerant of sulfasalazine

Ulcerative Colitis Agents

Drug	Manufacturer	Indication(s)	
		Treatment	Maintenance
sulfasalazine (Azulfidine®, Azulfidine EN-tabs®)	generic*, Pfizer	Mild 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 Agents

Drug	Manufacturer	Indication(s)	
		Treatment	Maintenance
Oral Delayed-Release Forms			
mesalamine delayed-release tablets (Asacol® HD)	generic, Allergan	Moderately active UC	--
mesalamine delayed-release capsules (Delzicol®)	generic, Allergan	Mild to moderately active UC in patients ≥ 5 years	Maintenance of remission of UC in adults
mesalamine MMX delayed-release tablets (Lialda®)	generic, Shire US	Mild to moderately active UC in pediatric patients ≥ 24 kg and adults	Maintenance of remission of mild to moderately active UC in adults

Ulcerative Colitis Agents

Drug	Manufacturer	Indication(s)	
		Treatment	Maintenance
mesalamine extended-release capsules (Pentasa®)	Shire US	Mild to moderately active UC	--
mesalamine extended-release capsules (Apriso®)	generic, Salix	--	Maintenance of remission of UC in adults
Rectal Forms			
budesonide rectal foam (Uceris®)	Salix	Mild to moderate active UC extending 40 cm from the anal verge	--

Ulcerative Colitis Agents

Drug	Manufacturer	Indication(s)	
		Treatment	Maintenance
mesalamine enemas (Rowasa®)	Meda/Mylan	Mild to moderately active distal UC, proctosigmoiditis, or proctitis	--
mesalamine enemas sulfite-free (sfRowasa®)	generic, Meda/Mylan	Mild to moderately active distal UC, proctosigmoiditis, or proctitis	--
mesalamine suppositories (Canasa®)	generic, Allergan	Active ulcerative proctitis	--
Oral Corticosteroids			
budesonide extended-release tablets (Uceris®)	generic, Santarus	Mild 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

Ulcerative Colitis Agents

- Second-line therapy with a course of oral or rectal steroids 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
- Several injectable tumor necrosis factor (TNF)-inhibitors (infliximab [Remicade], adalimumab [Humira], and golimumab [Simponi Aria]) are approved for inducing and maintaining clinical response/remission in patients with moderate to severe active UC who fail conventional therapy or who are considered at high-risk for colectomy

Ulcerative Colitis Agents

- Vedolizumab (Entyvio) is an intravenous (IV) integrin receptor antagonist indicated in adults for the treatment of moderately to severely active UC and moderately to severely active Crohn's disease
- Ustekinumab (Stelara) is approved for the treatment of adults with moderately to severely active UC.
- The oral Janus kinase (JAK) inhibitor tofacitinib (Xeljanz, Xeljanz XR) is indicated for adults with moderately to severely active UC, specifically for patients with an inadequate response or intolerance to TNF inhibitors

Ulcerative Colitis Agents

- The FDA has approved Zeposia (fingolimod) for the treatment of moderately to severely active ulcerative colitis (UC) in adults.
- Zeposia was already indicated for adults with relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease.

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
- 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 active UC who are intolerant or non-responsive to 5-ASA, oral budesonide MMX is recommended to induce remission
- Moderately active UC should be treated with oral 5-ASA or budesonide
- In patients with moderately to severely active UC, the ACG recommends induction of remission using systemic corticosteroids, anti-TNF therapy, vedolizumab, or tofacitinib

Ulcerative Colitis Agents

- Per the 2020 American Gastroenterological Association (AGA) practice guidelines, long-term management of patients with moderate to severe UC can include medications from the following classes: TNF-alpha antagonists, immunomodulators (e.g., thiopurines [azathioprine], methotrexate), the anti-integrin agent vedolizumab, and JAK inhibitors (e.g., tofacitinib)
- With the exception of corticosteroids or cyclosporine, if the agent selected for inducing remission is effective, it is usually continued as maintenance therapy
- Methotrexate monotherapy is suggested against use for induction and maintenance of remission

New Drug Reviews

Sarah Martinez, Pharm.D.

AHCCCS
Arizona Health Care Cost Containment System

New Products

- Azstarys (serdexmethylphenidate/dexmethylphenidate)
- Bylvay (odevixibat)
- Kerendia (finerenone)
- Livmarli (maralixibat)
- Livtencity (maribavir)
- Lybalvi (olanzapine/samidorphan)

New Products

- Opzelura (ruxolitinib)
- Qulipta (atogepant)
- Rezurock (belumosudil)
- Skytrofa (lonapegsomatropin-tcgd)
- Tavneos (avacopan)
- Tyrvaya (varenicline)

Azstarys (serdexmethylphenidate/dexmethylphenidate)

- Indicated for the treatment of ADHD in patients ≥ 6 years old.
- Available as oral capsules (serdexmethylphenidate/dexmethylphenidate) in the following strengths: 26.1 mg/5.2 mg, 39.2 mg/7.8 mg, 52.3 mg/10.4 mg
- The recommended starting dose is 39.2 mg/7.8 mg orally once daily in the morning
- The capsules can be taken with or without food and should be swallowed whole or opened and sprinkled onto applesauce or added to water.

Azstarys (serdexmethylphenidate/dexmethylphenidate)

- It carries a boxed warning for abuse and dependence, and has a Schedule II controlled classification as it contains dexmethylphenidate
- Contraindications:
  - Known hypersensitivity to serdexmethylphenidate, methylphenidate, or other components
  - Concomitant use of monoamine oxidase inhibitors (MAOIs) or within 14 days following discontinuation of a MAOI
- Adverse reactions:
  - Headache
  - Insomnia
  - Abdominal pain
  - Pharyngitis

Azstarys (serdexmethylphenidate/dexmethylphenidate)

- Warnings/precautions:
  - Potential for abuse/dependence
  - Serious cardiovascular reactions (e.g., sudden death, stroke, myocardial infarction)
  - Increases in blood pressure/heart rate
  - Psychiatric adverse reactions (e.g., exacerbation of psychosis, mania in bipolar disorder, psychotic/manic symptoms)
  - Priapism
  - Peripheral vasculopathy
  - Long-term suppression of growth

Azstarys (serdexmethylphenidate/dexmethylphenidate)

- The safety and efficacy was studied in a long- and short-term study to evaluate the safety and efficacy in children aged 6 to 12 years old with ADHD (combined, inattentive, or hyperactive/impulsive presentation) that was confirmed by the Mini International Neuropsychiatric Interview for Children and Adolescents (MINI-KID).
- Participants (n=150) were randomized 1:1 to receive either placebo or serdexmethylphenidate/dexmethylphenidate, with a dose optimization of 3 weeks, followed by the study period of 1- week as part of a phase 3, double-blind, multicenter, parallel, laboratory classroom study. Safety and efficacy assessments were performed at day 7.

Azstarys (serdexmethylphenidate/dexmethylphenidate)

- The least-squares mean change from baseline of the SKAMP-combined score taken on test day was -4.87 for the serdexmethylphenidate/dexmethylphenidate group and 0.54 for placebo (difference of -5.4; 95% confidence interval [CI] -7.1 to -3.7), showing improvement, in comparison to placebo.

Azstarys (serdexmethylphenidate/dexmethylphenidate)

- At the conclusion of the short-term study, a long-term, open-label study (n=238) was conducted for 12-months that included those who had completed the short-term study and new enrollees to gather safety data.
- A total of 154 patients finished treatment during the 12-month period.
- At the conclusion of the study, it was found that although participants had lower than expected increases in body weight and height, an occurrence common with stimulants, these results were deemed not clinically significant (z-score change < 0.5).
- It was also noted that due to the open-label and uncontrolled design of the study, any adverse reaction rates, could not be assessed as a causal relationship to treatment.

Bylvay (odevixibat)

- Indicated for the treatment of pruritus in patients 3 months of age and older with progressive familial intrahepatic cholestasis (PFIC)
- Bylvay may not be effective in PFIC type 2 patients with ABCB11 variants resulting in non-functional or complete absence of bile salt export pump protein (BSEP-3)
- The recommended dosage is 40 mcg/kg once daily. If there is no improvement in pruritus after 3 months, the dosage may be increased in 40 mcg/kg increments up to 120 mcg/kg once daily not to exceed a total daily dose of 6 mg
- Available as 200 mcg and 600 mcg oral pellets, as well as 400 mcg and 1200 mcg capsules

Bylvay (odevixibat)

- Warnings:
  - Liver Test Abnormalities
  - Fat-Soluble Vitamin Deficiency
  - Diarrhea
- Adverse Reactions
  - Liver test abnormalities
  - Abdominal pain
  - Fat-soluble vitamin deficiency
  - Diarrhea
  - Vomiting
- The approval of Bylvay was supported by data from PEDFIC 1 and PEDFIC 2, the largest, global, Phase 3 trials ever conducted in PFIC

Bylvay (odevixibat)

- PEDFIC1 was a randomized, double-blind, placebo-controlled study
- In this trial, Bylvay met both its pruritus and serum bile acid primary endpoints and was well tolerated with very low incidence of diarrhea/frequent bowel movements (9.5% of treated patients vs. 5.0% of placebo patients)
- PEDFIC 2 was a long-term, open-label Phase 3 extension study
- This trial reaffirmed Bylvay delivered sustained reductions in serum bile acids as well as improvements in pruritus assessments, growth and other markers of liver function in patients treated up to 48 weeks

Kerendia (Finerenone)

- Finerenone (Kerendia) is a non-steroidal mineralocorticoid receptor antagonist (MRA) indicated to reduce the risk of sustained estimated glomerular filtration rate (eGFR) decline, end stage kidney disease, cardiovascular death, non-fatal myocardial infarction, and hospitalization for heart failure in adult patients with chronic kidney disease (CKD) associated with type 2 diabetes (T2D).
- Available as 10 and 20 mg tablets
- Finerenone is contraindicated in patients concomitantly receiving strong CYP3A4 inhibitors and in patients with adrenal insufficiency.

Kerendia (finerenone)

- Serum potassium and eGFR should be measured prior to initiation of therapy; finerenone should not be initiated in patients with serum potassium > 5 mEq/L.
- Serum potassium should be monitored 4 weeks after initiation of therapy or dose adjustment and periodically throughout treatment.
- More frequent monitoring of serum potassium levels may be needed in patients at increased risk for hyperkalemia.

Kerendia (finerenone)

- For patients with eGFR ≥ 60 mL/min/1.73 m2, the recommended starting dose is 20 mg once daily.
- For patients with eGFR ≥ 25 to < 60 mL/min/1.73 m2, the recommended starting dose is 10 mg once daily. Use is not recommended in patients with an eGFR < 25 mL/min/1.73 m2.
- Adverse Reactions:
  - Hyperkalemia
  - Hyponatremia
  - Hypotension

Kerendia (finerenone)

- The safety and efficacy of finerenone were evaluated in the Finerenone in Reducing Kidney Failure and Disease Progression in Diabetic Kidney Disease (FIDELIO-DKD) trial, a phase 3, randomized, double-blind, placebo-controlled, multicenter trial of adult patients with CKD and T2D.
- At time of screening, eligible patients were required to have a serum potassium ≤ 4.8 mEq/L and be receiving background standard of care therapy, including an angiotensin-converting enzyme inhibitor (ACEI) and/or angiotensin receptor blocker (ARB).
- During the 4- to 16-week run-in period, background therapy was adjusted, including ACEI or ARB adjusted to the maximum tolerated labeled dose. After the run-in period, 5,734 eligible patients were randomized 1:1 to received oral finerenone or placebo.

Kerendia (finerenone)

- The primary efficacy outcome was a composite of kidney failure (defined as eGFR < 15 mL/min/1.73 m2, initiation of dialysis for ≥ 90 days, or kidney transplantation), a decrease of ≥ 40% eGFR from baseline for ≥ 4 weeks, or death from renal causes.
- The key secondary efficacy endpoint was a composite of death from cardiovascular causes, nonfatal myocardial infarction, nonfatal stroke, or hospitalization for heart failure.
- At a median follow-up of 2.6 years, the primary efficacy composite occurred at a lower rate in patients receiving finerenone compared to placebo (504 patients [17.8%] versus 600 patients [21.1%]; hazard ratio [HR], 0.82; 95% confidence interval [CI], 0.73 to 0.93; p=0.001).

Kerendia (finerenone)

- Similarly, the key secondary composite outcome occurred at a lower rate in patients receiving finerenone compared to placebo (367 patients [13%] versus 420 patients [14.8%]; HR, 0.86; 95% CI, 0.75 to 0.99; p=0.03); this effect was primarily due to a reduction in cardiovascular death, non-fatal myocardial infarction, and hospitalization for heart failure.

Kerendia (finerenone)

- The safety and efficacy of finerenone were also evaluated in the Finerenone in Reducing Cardiovascular Mortality and Morbidity in Diabetic Kidney Disease (FIGARO-DKD) trial, a phase 3, randomized, double-blind, placebo-controlled, multicenter clinical trial of adult patients with CKD and T2D.
- The patients enrolled were considered to be at high cardiovascular risk but previously excluded from or understudied in the FIDELIO-DKD trial.
- At time of screening, eligible patients were required to have a serum potassium ≤ 4.8 mEq/L and be receiving background standard of care therapy, including an angiotensin-converting enzyme inhibitor (ACEI) or angiotensin receptor blocker (ARB).

Kerendia (finerenone)

- During the run-in period, background therapy was adjusted, including ACEI or ARB adjusted to the maximum tolerated labeled dose.
- After the run-in period, 7,437 eligible patients were randomized 1:1 to receive oral finerenone or placebo.
- The primary efficacy outcome was a composite of death from cardiovascular causes, nonfatal myocardial infarction, nonfatal stroke, or hospitalization for heart failure.
- The key secondary efficacy outcome was a composite of kidney failure (defined as eGFR < 15 mL/min/1.73 m2, initiation of dialysis for ≥ 90 days, or kidney transplantation), a decrease of ≥ 40% eGFR from baseline for ≥ 4 weeks, or death from renal causes.

Kerendia (finerenone)

- During the follow-up period (median, 3.4 years), the primary outcome composite occurred at a lower rate in patients receiving finerenone compared to placebo (458 patients [12.4%] versus 519 patients [14.2%], respectively; HR, 0.87; 95% CI, 0.76 to 0.98; p=0.03); this was primarily due a lower incidence of hospitalization for heart failure in the finerenone arm (HR, 0.71; 95% CI, 0.56 to 0.9).
- The key secondary composite outcome occurred 350 finerenone patients (9.5%) versus 395 placebo patients (10.8%), which did not represent a significant decrease in the incidence (HR, 0.87; 95% CI, 0.76 to 1.01).
- Overall, the incidence of adverse effects was similar between the 2 groups; however, the incidence of hyperkalemia was higher with finerenone compared to placebo (10.8% versus 5.3%, respectively).

Livmarli (maralixibat)

- An ileal bile acid transporter (IBAT) inhibitor indicated for the treatment of cholestatic pruritus in patients ≥ 1 year of age with Alagille syndrome (ALGS).
- Available as 9.5 mg/mL oral solution
- Maralixibat should be initiated at 190 mcg/kg once daily for 1 week, then increased to 380 mcg/kg once daily, as tolerated. All doses should be administered 30 minutes prior to the first meal of the day. The maximum daily dose of maralixibat in patients > 70 kg is 28.5 mg (3 mL) daily.
- Maralixibat has no contraindications.

Livmarli (maralixibat)

- Warnings:
  - Liver test abnormalities
  - Fat-soluble vitamin deficiency
  - Gastrointestinal (GI) adverse reactions
- Providers should obtain baseline liver tests and monitor patients during treatment.
- Treatment interruption or a dose reduction may be considered for abnormalities in the absence of other causes, and treatment discontinuation should be considered in patients with recurrent or persistent liver test abnormalities.

Livmarli (maralixibat)

- Adverse Effects:
  - Diarrhea
  - Vomiting
  - Nausea
  - Bone Fractures
  - Abdominal Pain
  - GI Bleeding
  - Fat-soluble vitamin deficiency
- Drug Interactions:
  - Maralixibat may bind to bile acid binding resins (e.g., cholestyramine, colesevelam, colestipol) in the gut; bile acid binding resins should be administered ≥ 4 hours before or after maralixibat.
  - Maralixibat is an OATP2B1 inhibitor and may impact the oral absorption of OATP2B1 substrates (e.g., statins) in the GI tract. Additional monitoring may be needed.

Livmarli (maralixibat)

- A 48-week multinational study, assessed the efficacy of maralixibat in 31 pediatric patients with ALGS who had cholestasis and pruritis who weighed up to 50 kg.
- The trial consisted of an 18-week open-label treatment period, followed by a 4-week randomized, double-blind, placebo-controlled treatment-withdrawal period, and then followed by a 26-week open-label treatment period.
- Patients were then able to continue treatment in an open-label, long-term extension period.
- In the 18-week open-label treatment period, patients received 13 weeks of 380 mcg/kg/day following a 5-week dose titration.

Livmarli (maralixibat)

- At baseline, 28 patients (90.3%) had received ≥ 1 medication for pruritis, and all had a JAGGED1 mutation.
- The mean (standard deviation [SD]) baseline worst daily ItchRO(Obs) pruritus score was 3.1 (0.5). The mean (SD) post-18-week (pre-randomization) worst daily ItchRO(Obs) pruritus score was 1.4 (0.9).
- The 29 remaining patients were then randomized to either continue treatment or to placebo for weeks 19 through 22 (13 assigned maralixibat, 16 to placebo).

Livmarli (maralixibat)

- The primary outcome, the weekly average worst daily ItchRO(Obs) score, as assessed by the caregiver and evaluated using an analysis of covariance model, was generally maintained in the treatment group and returned to baseline in the placebo group.
- At week 22, the mean weekly average worst daily ItchRO(Obs) score was 1.6 (95% confidence interval [CI]; 1.1 to 2.1) in the maralixibat group compared to 3 (95% CI, 2.6 to 3.5) in the placebo group.
- The mean change from week 18 to week 22 in the weekly average worst daily ItchRO(Obs) score was 0.2 (95% CI, -0.3 to 0.7) in the maralixibat group compared to 1.6 (95% CI, 1.2 to 2.1), with a mean difference between the groups of -1.4 (95% CI, -2.1 to -0.8).

Livmarli (maralixibat)

- All patients completed the randomized, treatment-withdrawal phase and continued to the 26-week, open-label treatment period.
- Upon reentry to open-label treatment, both groups had similar pruritis scores by week 28.

Livtencity (maribavir)

- Indicated for the treatment of adults and pediatric patients (12 years of age and older and weighing at least 35 kg) with post-transplant cytomegalovirus (CMV) infection/disease that is refractory to treatment (with or without genotypic resistance) with ganciclovir, valganciclovir, cidofovir or foscarne
- Dosage is 400 mg orally twice daily. It is available as 200 mg tablets
- Warnings:
  - Risk of Reduced Antiviral Activity When Co-administered with Ganciclovir and Valganciclovir (Coadministration is not recommended)
  - Virologic failure (which can occur during and after treatment. Resistance should be checked if patient does not respond to treatment)
  - Risk of Adverse Reactions or Loss of Virologic Response Due to Drug Interactions (Drugs that are strong inducers of CYP3A4 may result in reduced virologic response of Livtencity)

Livtencity (maribavir)

- Use with Immunosuppressant Drugs (LIVTENCITY has the potential to increase the drug concentrations of immunosuppressant drugs that are CYP3A4 and/or P-glycoprotein substrates)

- Adverse reactions:
  - Taste disturbance
  - Diarrhea
  - Fatigue
  - Nausea
  - Vomiting
- SOLSTICE was a multicenter, randomized, open-label, active-controlled superiority trial
- The objective was to assess the efficacy and safety of treatment with Livtencity compared investigator assigned treatment, IAT, (conventional antiviral therapy)

Livtencity (maribavir)

- Trial subjects were 352 hematopoietic stem cell transplant and solid organ transplant recipients with CMV infection refractory, with or without resistance, to one or a combination of the conventional antiviral therapies: ganciclovir, valganciclovir, foscarnet or cidofovir
- Patients underwent a 2-week screening period, followed by randomization 2:1 to Livtencity (400 mg, twice daily) or IAT (as dosed by the investigator) for up to 8-weeks
- After completion of the treatment period, subjects entered a 12-week follow-up phase
- Overall, more than twice the proportion of patients achieved confirmed CMV DNA level <LLOQ (lower limit of quantification, i.e. <137 IU/mL) at Week 8 (end of treatment phase), the study's primary endpoint, with Livtencity (56%), compared to those treated with conventional antiviral therapies (24%)

Lybalvi (olanzapine/samidorphan)

- Indicated for treatment of:
  - 1) schizophrenia in adults
  - 2) bipolar I disorder in adults

    a) for the acute treatment of manic or mixed episodes as monotherapy and as adjunct to lithium or valproate

    b) for maintenance monotherapy treatment

- Supplied as oral tablets (olanzapine/samidorphan): 5 mg/10 mg, 10 mg/10 mg, 15 mg/10 mg, and 20 mg/10 mg

Lybalvi (Olanzapine/samidorphan)

- Dosing:
  - Max dose for all indications is 20 mg/10 mg once daily
  - Schizophrenia - initial dose 5 mg/10 mg or 10 mg/10 mg once daily; adjustments at weekly intervals of 5 mg
  - Bipolar I disorder (monotherapy) - initial dose 10 mg/10 mg or 15 mg/10 mg once daily; titration at intervals of no less than 24 hours in 5 mg increases/decreases
  - Bipolar I disorder (adjunct to lithium or valproate) - initial dose 10 mg/10 mg once daily; adjustments at weekly intervals in 5 mg

Lybalvi (Olanzapine/samidorphan)

- Due to the samidorphan (an opioid antagonist) component, Lybalvi may precipitate severe opioid withdrawal in patients who are physiologically dependent on opioids; therefore, use of Lybalvi is contraindicated in patients who are using opioids and in those who are undergoing acute opioid withdrawal.
- Lybalvi carries a warning for vulnerability to life-threatening opioid overdose due to potential attempts at overcoming the samidorphan blockade; those with a history of chronic opioid use, before treatment, may have a reduced opioid tolerance if Lybalvi is interrupted or discontinued.

Lybalvi (Olanzapine/samidorphan)

- Lybalvi carries a boxed warning for increased mortality in elderly patients with dementia-related psychosis, and it is not approved for treating patients with dementia-related psychosis.
- It also carries a warning for cerebrovascular adverse reactions, including stroke, in elderly patients with dementia-related psychosis (olanzapine component).

Lybalvi (Olanzapine/samidorphan)

- The following additional warnings are also attributed to the olanzapine component, some of which could lead to fatal events:
  - Neuroleptic malignant syndrome (NMS)
  - Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS)
  - Metabolic changes (e.g., hyperglycemia, diabetes mellitus, dyslipidemia, body weight gain)
  - Tardive dyskinesia (potentially irreversible)
  - Orthostatic hypotension and syncope; falls, fractures, or other injuries
  - Leukopenia, neutropenia, and agranulocytosis
  - Dysphagia leading to esophageal dysmotility and aspiration

Lybalvi (Olanzapine/samidorphan)

- The following additional warnings are also attributed to the olanzapine component, some of which could lead to fatal events:
  - Seizures (greatest risk in those with past history or who have conditions lowering seizure threshold)
  - Potential for cognitive and motor impairment due to somnolence (caution with operating hazardous machinery)
  - Body temperature dysregulation
  - Anticholinergic effects
  - Hyperprolactinemia leading to inhibited reproductive function (resulting in galactorrhea, amenorrhea, gynecomastia, impotence, decreased bone density).

Lybalvi (Olanzapine/samidorphan)

- Adverse reactions:
  - Weight Increase
  - Somnolence
  - Increased appetite
  - Blood creatine phosphokinase increase
  - Dry mouth
  - Headache
  - Waist circumference increase

Lybalvi (Olanzapine/samidorphan)

- Lybalvi was approved via the 505(b)(2) pathway, hence at least a portion of the data supporting its approval may have been derived from another formulation/another manufacturer; efficacy in adults with bipolar I disorder was previously established based on adequate and well-controlled studies of orally administered olanzapine.
- Efficacy in schizophrenia was based on previously conducted studies evaluating oral olanzapine in adults and a 4-week, randomized, double-blind, placebo- and active-controlled study (ENLIGHTEN-1) conducted in adults who met Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) criteria for schizophrenia and were experiencing an acute exacerbation

Lybalvi (Olanzapine/samidorphan)

- At week 4, a statistically significant improvement in the change from baseline in PANSS total score was seen in Lybalvi-treated patients compared to placebo with a least squares mean (LSM) change in the placebo-subtracted difference of -6.4 (95% confidence interval [CI], -10 to -2.8); in comparison in the olanzapine arm, the placebo-subtracted difference was -5.3 (95% CI, -8.9 to -1.7).
- At week 4, a statistically significant improvement in the secondary endpoint, CGI-S score, was also seen in Lybalvi-treated patients compared to placebo.

Lybalvi (Olanzapine/samidorphan)

- A separate phase 3, double-blind, 24-week study (ENLIGHTEN-2) was conducted to evaluate the effect on weight in adults who met DSM-5 criteria for schizophrenia.
- The coprimary endpoints were percentage change from baseline in body weight and the proportion of patients who gained ≥ 10% body weight by week 24.
- Lybalvi resulted in significantly less weight gain than olanzapine (LSM percentage weight change from baseline 4.21% versus 6.59%, respectively; olanzapine-subtracted difference -2.38%; 95% CI, -3.9 to -0.9).

Lybalvi (Olanzapine/samidorphan)

- In addition, significantly less patients in the Lybalvi group compared with the olanzapine group had ≥ 10% weight gain (17.8% versus 29.8%; difference -13.7%; 95% CI, -22.8 to -4.6; odds ratio 0.5; number-needed-to-treat 7.29).
- Improvement in schizophrenia symptoms were similar between study arms, and patients in the Lybalvi group demonstrated smaller increases in waist circumferences compared with olanzapine-treated patients; metabolic changes were small and comparable between study arms.

Opzelura (ruxolitinib)

- Indicated for the short-term and non-continuous chronic treatment of mild to moderate atopic dermatitis (AD) in non-immunocompromised patients ≥ 12 years of age whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable
- Ruxolitinib (Opzelura) is the first and only FDA-approved topical JAK inhibitor in the US; oral ruxolitinib is also available from Incyte, marketed as Jakafi
- Available as a 1.5% cream in a 60-gram tube
- Directions are to apply a thin layer twice daily to affected areas of up to 20% of the body surface area (BSA); maximum dose is 60 grams per week; re-evaluate therapy if signs and symptoms do not improve within 8 weeks

Opzelura (ruxolitinib)

- There are no contraindications associated with use of ruxolitinib; however, it carries multiple boxed warnings associated with use of JAK inhibitors for inflammatory conditions including risk of serious infections, higher rate of all-cause mortality, occurrence of lymphoma and other malignancies, higher rate of major adverse cardiovascular events (MACE), and increased incidence of thrombosis.

Opzelura (ruxolitinib)

- Warnings:
  - Thrombocytopenia
  - Neutropenia
  - Anemia
  - Lipid elevations

- Adverse reactions
  - Nasopharyngitis
  - Bronchitis
  - Tonsillitis rhinorrhea
  - Diarrhea
  - Ear infection
  - Folliculitis
  - Eosinophil count increase
  - Urticaria

Opzelura (ruxolitinib)

- Efficacy and safety of ruxolitinib cream was evaluated in 2 identical, double-blind, randomized, vehicle-controlled, phase 3 trials (TRuE-AD1: and TRuE-AD2).
- The primary efficacy endpoint was IGA treatment success (IGA-TS) at week 8, defined as IGA score of 0 (clear) or 1 (almost clear) and ≥ 2-grade improvement from baseline.
- More patients in both trials achieved the primary endpoint with 0.75% ruxolitinib cream (50% and 39%, TRuE-AD1 and TRuE-AD2, respectively) and 1.5% ruxolitinib cream (53.8% and 51.3%) compared to the vehicle cream (15.1% and 7.6%; all $p<0.0001$).

Opzelura (ruxolitinib)

- During the 8-week study period, ruxolitinib cream was well tolerated; long-term safety studies are ongoing.
- The ruxolitinib 0.75% strength is not approved by the United States (US) Food and Drug Administration (FDA) at this time.

Qulipta (atogepant)

- A calcitonin gene-related peptide (CGRP) receptor antagonist indicated for preventive treatment of episodic migraine in adults
- Available as 10 mg, 30 mg, and 60 mg oral tablets
- Dosing is 10 mg, 30 mg, or 60 mg orally once daily; dose adjustments for renal impairment and concomitant use with select CYP3A4 inhibitors or inducers or OATP inhibitors
- There are no contraindication or warnings for use of atogepant.

Qulipta (atogepant)

- Adverse reactions:
  - Nausea
  - Fatigue/somnolence
  - Weight loss
  - Constipation
  - Elevated transaminase levels
- Drug interactions:
  - Strong CYP3A4 inhibitors
  - Moderate and strong CYP3A4 inducers
  - Organic-anion-transporting polypeptide (OATP) inhibitors

Qulipta (atogepant)

- Two randomized, multicenter, double-blind, placebo-controlled studies (Study 1, n=910; Study 2, n=652) enrolled adults with a ≥ 1-year history of migraine with or without aura, as based on the International Classification of Headache Disorders (ICHD-3) diagnostic criteria.
- Eligible patients experienced 4 to 14 monthly migraine days (MMD).
- The mean MMD at baseline was 8 days in each study. Mean age was 42 years (Study 1) and 40 years (Study 2). The majority of patients were female.
- The primary efficacy endpoint in both studies was the change from baseline in the mean MMD during the 12-week treatment period.

Qulipta (atogepant)

- The mean change from baseline in MMD for atogepant 10 mg, 30 mg, and 60 mg and placebo in Study 1 was -3.7, -3.9, -4.2, and -2.5 days, respectively ($p<0.001$ for all doses versus placebo), and in Study 2 was -4, -3.8, -3.6, and -2.8 days, respectively ($p=0.024$, $p=0.039$, and $p=0.039$, respectively, versus placebo).
- Similarly, significant changes in monthly headache days were seen with atogepant in each study.
- In Study 1, significant improvement in other secondary endpoints were also seen with all doses of atogepant compared to placebo; these endpoints included monthly acute medication use, percentage of responders that achieved ≥ 50% reduction in MMD, and quality of life measures.

Rezurock (belumosudil)

- Indicated for the treatment of adult and pediatric patients 12 years and older with chronic graft-versus-host disease (cGVHD) after failure of at least two prior lines of systemic therapy
- Dosage is 200 mg taken orally once daily. It is available as 200 mg tablets
- Warning:
  - Embryo-Fetal Toxicity
- Drug Interactions
  - Strong CYP3A Inducers and Proton Pump Inhibitors (increase Rezurock dosage to 200 mg twice daily)

Rezurock (belumosudil)

- Adverse Reactions (including laboratory abnormalities)
  - Infections
  - Nausea
  - Dyspnea
  - Edema
  - Abdominal Pain
  - Headache
  - Increased Gamma Glutamyl Transferase
  - Hypertension
  - Asthenia
  - Diarrhea
  - Cough
  - Hemorrhage
  - Musculoskeletal Pain
  - Decreased Phosphate
  - Decreased Lymphocytes

Rezurock (belumosudil)

- ROCKstar was a randomized, open-label, multicenter trial of patients with cGVHD who had received two to five prior lines of systemic therapy
- There were 65 patients treated with Rezurock 200 mg taken orally once daily
- The median time from cGVHD diagnosis was 25.3 months and 48% of patients had four or more organs involved
- Patients had cycled through a median of 3 prior lines of systemic therapy and 78% were refractory to their last therapy
- Rezurock 200 mg QD achieved an Overall Response Rate (ORR) of 75% through Cycle 7 Day 1 of treatment, with 6% achieving a complete response and 69% achieving a partial response

Rezurock (belumosudil)

- The median time to first response was 1.8 months
- 62% of responders did not require new systemic therapy for at least 12 months following response
- The median duration of response, calculated from first response to progression, death, or new systemic therapies for chronic GVHD, was 1.9 months
- ORR results were supported by clinically meaningful improvement from baseline in the Lee Symptom Scale (LSS) score, a chronic GVHD symptom measurement, in 52% of patients through Cycle 7 Day 1 of treatment

Skytrofa (lonapegsomatropin-tcgd)

- Indicated for the treatment of pediatric patients ≥ 1 year old who weigh ≥ 11.5 kg and have growth failure due to inadequate secretion of endogenous growth hormone (GH)
- Lonapegsomatropin-tcgd (Skytrofa) is a long-acting prodrug of a human GH (HGH; somatropin) made through recombinant DNA technology using *Escherichia coli*.
- Lonapegsomatropin-tcgd contains somatropin conjugated to a methoxypolyethylene glycol carrier via a proprietary TransCon™ linker; this results in a pegylated form of human GH

Skytrofa (lonapegsomatropin-tcgd)

- Available as a lyophilized powder available in single-dose, dual-chamber, prefilled cartridges containing drug and diluent, water for injection, in the following strengths: 3 mg, 3.6 mg, 4.3 mg, 5.2 mg, 6.3 mg, 7.6 mg, 9.1 mg, 11 mg, and 13.3 mg
- For treatment-naïve patients and patients switching from daily somatropin: 0.24 mg/kg body weight once-weekly via subcutaneous (SC) injection into the abdomen, buttock, or thigh; individualize and titrate based on response
- Discontinue therapy once epiphyseal fusion has occurred

Skytrofa (lonapegsomatropin-tcgd)

- Contraindications:
  - Acute critical illness (e.g., after open heart surgery, abdominal surgery or multiple accidental trauma, or those with acute respiratory failure due to the increased risk of mortality with use of somatropin)
  - Hypersensitivity to somatropin or any of the excipients
  - Children with closed epiphyses
  - Active malignancy due to the risk of malignancy progression
  - Active proliferative or severe non-proliferative diabetic retinopathy as treatment with somatropin may worsen this condition

Skytrofa (lonapegsomatropin-tcgd)

- Contraindications:
  - Prader-Willi syndrome
  - Patients who are severely obese, have a history of upper airway obstruction or sleep apnea or have severe respiratory impairment due to the risk of sudden death

Skytrofa (lonapegsomatropin-tcgd)

- Warnings/Precautions:
  - Severe hypersensitivity reactions
  - Including anaphylactic reactions and angioedema
  - Increased risk of neoplasms (preexisting malignancy should be inactive, and its treatment should be completed before starting therapy; risk of second neoplasms in pediatric patients; new malignancy during treatment)
  - Glucose intolerance and diabetes mellitus
  - Reversible intracranial hypertension (e.g., papilledema, visual changes, headache, nausea, and/or vomiting)

Skytrofa (lonapegsomatropin-tcgd)

- Warnings/Precautions:
  - Transient and dose-dependent fluid retention (e.g., edema, arthralgia, myalgia, nerve compression syndromes)
  - Hypoadrenalism
  - Hypothyroidism
  - Slipped capital femoral epiphysis (onset of a limp or persistent hip/knee pain)
  - Progression of preexisting scoliosis
  - Pancreatitis
  - Lipoatrophy

Skytrofa (lonapegsomatropin-tcgd)

- Warnings/Precautions:
  - Sudden death in pediatric patients with Prader-Willi syndrome
  - Laboratory tests (e.g., phosphate, alkaline phosphatase, parathyroid hormone may increase)

Skytrofa (lonapegsomatropin-tcgd)

- Monitoring:
  - Monitor glucose in all patients, especially in those with risk factors for type 2 diabetes mellitus (T2DM) (e.g., obesity or a family history)
  - When starting therapy, monitor patients with preexisting type 1 diabetes mellitus (T1DM), T2DM, or impaired glucose tolerance with adjustment of antihyperglycemic drugs as warranted
  - Perform fundoscopic examination prior to starting therapy to exclude preexisting papilledema and reevaluate periodically thereafter
  - Monitor for decreased serum cortisol levels and/or glucocorticoid dose increases in those with hypoadrenalism

Skytrofa (lonapegsomatropin-tcgd)

- Monitoring:
  - Periodic thyroid function tests and start/adjust thyroid hormone replacement therapy

- Drug Interactions:
  - Glucocorticoid therapy
  - Cytochrome P450-metabolized drugs
  - Oral estrogen
  - Insulin and/or other antihyperglycemic agents

Skytrofa (lonapegsomatropin-tcgd)

- Adverse effects:
  - Viral infection
  - Cough
  - Hemorrhage
  - Abdominal pain
  - Pyrexia
  - Nausea and vomiting
  - Diarrhea
  - Arthralgia and arthritis
  - Laboratory changes: phosphate and alkaline level elevation

Skytrofa (lonapegsomatropin-tcgd)

- A multicenter, global, randomized, open-label, active-controlled, parallel-group phase 3 study evaluated treatment-naïve, prepubertal pediatric patients with GHD across 52 weeks.
- Patients were randomized 2:1 to receive either lonapegsomatropin-tcgd at a dose of 0.24 mg/kg/week (n=105) or an equivalent weekly dose of somatropin (Genotropin), administered daily (n=56).

Skytrofa (lonapegsomatropin-tcgd)

- At 52 weeks, the primary endpoint of annualized height velocity (AHV) for lonapegsomatropin-tcgd was found to be non-inferior and superior to that observed with daily somatropin (least squares mean [LSM] AHV, 11.2 cm/year versus 10.3 cm/year, respectively; treatment difference, 0.9; 95% confidence interval [CI], 0.2 to 1.5, P=0.009).
- The secondary endpoint of change from baseline in height SDS at week 52 was also significantly improved with lonapegsomatropin-tcgd compared to daily somatropin (LSM height SDS, 1.1 versus 0.96; P=0.01). Safety (adverse events, tolerability, and immunogenicity) were comparable between study arms.

Tavneos (avacopan)

- Avacopan (Tavneos) is a complement 5a receptor (C5aR) antagonist indicated as an adjunctive treatment of adult patients with severe active anti-neutrophil cytoplasmic autoantibody (ANCA)-associated vasculitis (granulomatosis with polyangiitis [GPA] and microscopic polyangiitis [MPA]) in combination with standard therapy including glucocorticoids.
- Avacopan does not eliminate glucocorticoid use.
- Available as a 10 mg oral capsule
- Avacopan is contraindicated in patients with a serious hypersensitivity reaction to avacopan or to any of the excipients.

Tavneos (avacopan)

- Drug interactions:
  - Strong and moderate CYP3A4 inducers
  - Strong CYP3A4 inhibitors
  - CYP3A4 substrates

Tavneos (avacopan)

- Adverse effects:
  - Nausea
  - Hypertension
  - Vomiting
  - Fatigue
  - Dizziness
  - Headache
  - Diarrhea
  - Rash
  - Upper abdominal pain
  - Blood creatinine increased

Tavneos (avacopan)

- The safety and efficacy of avacopan was evaluated in a double-blind, active-controlled, phase 3 clinical trial.
- All patients in both the avacopan and prednisone treatment groups received 1 of the following standard immunosuppressive regimens: intravenous (IV) cyclophosphamide for 13 weeks followed by oral azathioprine (or mycophenolate mofetil) from week 15 onwards (31%); oral cyclophosphamide for 14 weeks followed by azathioprine (or mycophenolate mofetil) from week 15 onwards (4%); or IV rituximab once a week for 4 weeks without azathioprine or mycophenolate mofetil (65%).

Tavneos (avacopan)

- The primary endpoints were disease remission at week 26 and sustained disease remission at week 52.
- The primary endpoint of disease remission was defined as BVAS of 0 and no use of glucocorticoids for the treatment of ANCA-associated vasculitis from week 22 to week 26.

Tavneos (avacopan)

- At week 26, 72.3% achieved disease remission in the avacopan group, and 70.1% in the prednisone group achieved disease remission (treatment difference, 3.4%; 95% confidence interval [CI], -6 to 12.8; $p<0.001$ for noninferiority; $p=0.24$ for superiority).
- The primary endpoint of sustained disease remission was defined as remission at week 26 and week 52 without relapses between week 26 and week 52.
- Remission at week 52 was defined as a BVAS of 0 and no use of glucocorticoids for the treatment of ANCA-associated vasculitis from week 48 to week 52.

Tavneos (avacopan)

- In the avacopan group, 65.7% (95% CI, 57.9 to 72.8) achieved sustained remission compared to 54.9% (95% CI, 46.9 to 62.6) in the prednisone group (treatment difference, 12.5%; 95% CI, 2.6 to 22.3; p<0.001 for noninferiority; p=0.007 for superiority) at week 52.
- Based on the clinical trial, avacopan was noninferior to prednisone taper for remission at week 26 and superior for sustained remission at week 52.
- The secondary endpoints included glucocorticoid-induced toxicity, health-related quality of life, estimated glomerular filtration rate (eGFR) change from baseline, and urinary albumin:creatinine ratio (UACR) change from baseline.

Tyrvaya (varenicline)

- Indicated for the treatment of the signs and symptoms of dry eye disease (DED) in adults
- Available as a nasal solution; 0.03 mg base (0.05 mL)/spray (supplied as a carton containing 2 bottles of nasal spray; each bottle delivers 15 days supply (60 sprays)
- Directions are to administer one spray in each nostril twice daily (approximately 12 hours apart); prime with 7 actuations before first use, re-prime with 1 actuation if not used for > 5 days

Tyrvaya (varenicline)

- Varenicline nasal spray has no contraindications, warnings, or drug interactions listed in product labeling
- Adverse effects:
  - Sneezing Cough
  - Throat irritation Instillation-site irritation

Tyrvaya (varenicline)

- ONSET-1 and ONSET-2 both multicenter, randomized, double-blind, vehicle-controlled trials, supported efficacy of varenicline for approval for dry eye disease (DED).
- In ONSET-1, patients were randomized 1:1:1:1 to varenicline 0.006 mg, varenicline 0.03 mg, varenicline 0.06 mg, or vehicle as 1 spray in each nostril twice daily. In ONSET-2, patients were randomized 1:1:1 to varenicline 0.03 mg, varenicline 0.06 mg, or vehicle as 1 spray in each nostril twice daily.

Tyrvaya (varenicline)

- The primary endpoint was the percentage of patients who achieved ≥ 10 mm increase in Schirmer's score from baseline.
- At 28 days in ONSET-1, 52% of those treated with varenicline 0.03 mg in each nostril twice daily compared to 14% of those treated with placebo achieved the primary endpoint (proportion difference, 38%; 95% confidence interval [CI], 21 to 56; p<0.01).
- At 28 days in ONSET-2, 47% of those treated with varenicline 0.03 mg in each nostril twice daily compared to 28% of those treated with placebo achieved the primary endpoint (proportion difference, 20%; 95% CI, 11 to 28; p<0.01).

Tyrvaya (varenicline)

- At 28 days in ONSET-1, the mean change in Schirmer's score in those treated with varenicline 0.03 mg in each nostril twice daily was 11.7 mm compared to 3.2 mm in those treated with placebo.
- At 28 days in ONSET-2, the mean change in Schirmer's score in those treated with varenicline 0.03 mg in each nostril twice daily was 11.3 mm compared to 6.3 mm in those treated with placebo.

P&T Requests

- ADD CONTENT



Executive Session

Public Therapeutic Class Votes

P&T Meeting Dates

- **Future Meeting Date:**
  - May 24, 2022