Pulmonary and Critical Care Medication Update 2023

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19th Annual
Pulmonary, Critical Care, and Sleep Medicine Conference
Omaha, Nebraska, September 9, 2023

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Faculty Disclosure

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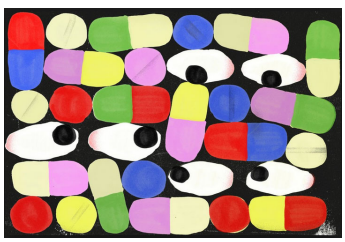
Mark A. Malesker, Pharm.D.

Dr. Malesker has listed no financial interest/arrangement that would be considered a conflict of interest



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Objectives

3

- Recognize newly approved pharmaceutical products and significant new dosage forms
- Discuss the indications, contraindications, dosage, drug interaction potential, and side effect potential for each agent
- Identify the place in therapy for each agent

3

Audience Question #1

4

- How many new novel medications were FDA approved in 2022 ?

- A. 27
- B. 37
- C. 48
- D. 59

4

Audience Question #2

5

- What is the indication for mavacamten (Camzyos) ?

- A. Obstructive hypertrophic cardiomyopathy
- B. Prostate cancer
- C. Resistant HIV
- D. Type 2 diabetes

5

Audience Question #3

6

- What is the mechanism of action for daridorexant (Quviviq)

- A. Antihistamine receptor antagonist
- B. Benzodiazepine receptor agonist
- C. Melatonin receptor agonist
- D. Orexin receptor antagonist

6

Drug Shortages: National Security Risk

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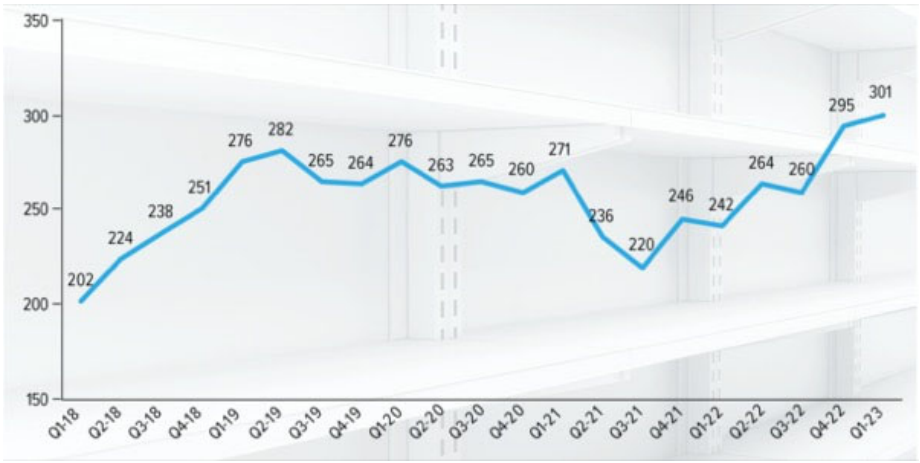

https://www.pharmacypracticenews.com/aimages/2023/PPN0723_022a_10088_600.jpg

7

2022 Drug Approvals

8

- The FDA approved 37 novel new drugs and biologics
  - Average of 43 for 2013-2022
- First in class (20/37) 54%
  - Drugs with a new and unique mechanism for treating a medical condition
- Orphan drugs (20/37) 54%
  - Drugs approved for small populations of patients with rare diseases (200,000 or fewer Americans)
  - 6800 rare diseases identified affecting 30 million people
- Breakthrough (13/37) 35%
  - Drugs for serious or life-threatening diseases for which there is unmet need and for which there is preliminary clinical evidence demonstrating that the drug may result in substantial improvement on a clinically significant endpoint

www.fda.gov/drugs

8

2022 Drug Approvals

9

- Fast track (12/37) 32%
  - Drugs that have potential to address unmet medical needs, speeds new development and review
- Priority review (21/37) 57%
  - A drug is given priority review if there is a potential to provide a significant advance in existing medical care, reviewed within eight months (standard 12 months)
- Accelerated approval (6/37) 16%
  - Early approval based on markers that predict a reasonable benefit, with more testing to confirm clinical benefit after approval

www.fda.gov/drugs

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2022 Drug Approvals

10

- First cycle (28/37) 76%
  - Drugs that were approved without additional information that could delay approval and lead to another cycle of review
- First approved in U.S. (25/37) 68%
  - Drugs that were approved in the United States before approved in another country

www.fda.gov/drugs

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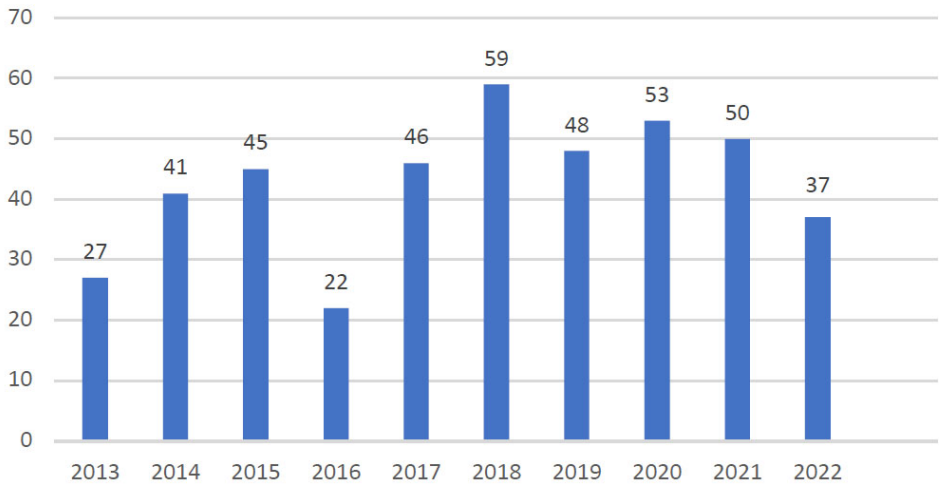
Novel Drug Approvals 2013-2022



www.fda.gov

11

2022 Drug Approvals (1)

12

Brand	Generic	Description
Amvuttra	Vutrisiran	Polyneuropathy of hereditary transthyretin-mediated amyloidosis
Briumvi	Ublituximab-xiiy	Multiple sclerosis
Camzyos	Mavacamten	Obstructive hypertrophic cardiomyopathy
Cibinqo	Abrocitinib	Atopic dermatitis
Daxxify	Daxibotulinumtoxin Alanm	Severe glabellar lines
Elahere	Mirvetuximab soravtansine-gynx	Ovarian cancer

www.fda.gov

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2022 Drug Approvals (2)

13

Brand	Generic	Description
Elucirem	Gadopiclenol	Contrast agent
Enjaymo	Sutimlimab-jome	Cold agglutinin disease
Imjudo	Tremelimumab-actl	Hepatocellular carcinoma
Kimmtrak	Tebentafusp-tebn	Uveal melanoma
Krazati	Adagrasib	Small cell lung cancer
Lunsumio	Mosunetuzumab-axgb	Refractory follicular lymphoma
Lytgobi	Futibatinib	Intrahepatic cholangiocarcinoma

www.fda.gov

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2022 Drug Approvals (3)

14

Brand	Generic	Description
Mounjaro	Tirzepatide	Diabetes
Nexobrid	Anacaulase-bcdb	Eschar removal associated with thermal burns
Omlonti	Omidenepag isopropyl	Open angle glaucoma or ocular hypertension
Opdualag	Nivolumab and relatlimab-rmbw	Melanoma
Pluvicto	Lutetium Lu 177 vipivotide tetraxetan	Prostate cancer
Pyrukynd	Mitapivat	Pyruvate kinase deficiency
Quviviq	Daridorexant	Insomnia

www.fda.gov

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2022 Drug Approvals (4)

15

Brand	Generic	Description
Relyvrio	Sodium phenylbutyrate and taurosodiol	Amyotrophic lateral sclerosis
Rezlidhia	Olutasidenib	Acute myeloid leukemia
Rolvedon	Eflapegrastim-xnst	Chemotherapy induced neutropenia
Sotyktu	Deucravacitinib	Plaque psoriasis
Spevigo	Spesolimab-sbzo	Pustular psoriasis flares
Sunlenca	Lenacapavir	HIV infections
Tecvayli	Teclistamab-cqyv	Multiple myeloma

www.fda.gov

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2022 Drug Approvals (5)

16

Brand	Generic	Description
Terlivaz	Terlipressin	Hepatorenal syndrome
Tyvaso	Trepostinil	Pulmonary hypertension
Tzield	Teplizumab-mzwv	Stage 3 type 1 diabetes
Vabysmo	Faricimab-svoa	Macular degeneration and diabetic macular edema
Vivjoa	Oteseconazole	Recurrent vulvovaginal candidiasis
Vonjo	Pacritinib	Myelofibrosis
Voquezna Triple Pak	Vonoprazan, amoxicillin, Clarithromycin	*H. pylori* infection

www.fda.gov

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2022 Drug Approvals (6)

17

Brand	Generic	Description
Vtama	Tapinarof	Plaque psoriasis
Xenoview	Hyperpolarized Xe-129	Contrast agent
Xenpozyme	Olipudase alfa-rpcp	Acid Sphingomyelinase Deficiency (ASMD)
Ztalmy	Ganaxolone	Seizures in cyclin-dependent kinase-like 5 deficiency disorder

www.fda.gov

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2022 New Indications (1)

18

Brand	Generic	Description
Cytalux	Pafolacianine	Pulmonary nodules
Dupixent	Dupilumab	Eosinophilic esophagitis
Dupixent	Dupilumab	Prurigo nodularis
Enhertu	Fam-trastuzumab derucxtecan-nxki	HER2-low breast cancer
Fintepla	Felfluramine	Lennox-Gastaut syndrome
Imcivree	Setmetanotide	Bardet-Biedl syndrome
Imfinzi	Durvalumab	Hepatocellular carcinoma

www.fda.gov

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2022 New Indications (2)

19

Brand	Generic	Description
Imjudo	Tremelimumab-actl	Non-small cell lung cancer
Jardiance	Empagliflozin	Reduce cardiovascular death and hospitalization for heart failure
Lynparza	Olabarib	HER2-negative early breast cancer
Nubeqa	Darolutamide	Prostate cancer
Olumiant	Baricitinib	COVID-19
Olumiant	Baricitinib	Alopecia areata

www.fda.gov

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2022 New Indications (3)

20

Brand	Generic	Description
Opdivo	Nivolumab	Non-small cell lung cancer
Opzelura	Ruxolitinib	Nonsegmental vitiligo
Pemazyre	Pemigatinib	Myeloid and lymphoid neoplasms
Retevmo	Selpercatinib	Metastatic solid tumors
Rinvoq	Upadacitinib	Ulcerative colitis
Skyrizi	Risankizumab-rzaa	Crohn's disease
Pedmark	Sodium thiosulfate	Reduce ototoxicity with cisplatin

www.fda.gov

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2022 New Indications (4)

21

Brand	Generic	Description
Tafinlar + Mekinist	Dabrafenib + Trametinib	Mutated solid tumors
Tymlos	Abaloparatide	Osteoporosis in males
Vidaza	Azacitidine	Juvenile myelomonocytic leukemia
Vijoice	Alpelisib	Overgrowth spectrum
Xalkori	Crizotinib	Myofibroblastic tumors

www.fda.gov

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Selected 2022 New Formulations (1)

22

Brand	Generic	Description
Adlarity	Donepezil	Transdermal patch for Alzheimer's dementia
Auvelity	Dextromethorphan/ bupropion	Depression
Aspruzyo Sprinkle	Ranolazine	ER formulation for angina
Dapzura RT	Daptomycin	New formulation
Furoscix	Furosemide	Single use SC infusion
Igalmi	Dexmedetomidine	SL film formulation
Konvomep	Omeprazole/sodium bicarbonate	Acid suppression

www.fda.gov

22

Selected 2022 New Formulations (2)

23

Brand	Generic	Description
Ryaltris	Olopatadine/ mometasone	Allergic rhinitis
Tadliq	Tadalafil	Oral suspension
Zoryve	Roflumilast	Topical for plaque psoriasis

www.fda.gov

23

2022 Drug Withdrawals

24

Brand	Generic	Description
Ukoniq	Umbralisib	Increased risk of death
Zelnorm	Tegaserod	Removed for business reasons, not safety or efficacy

www.fda.gov

24

2023 Drug Approvals (1)

25

Brand	Generic	Description
Leqembi	Lecanemab-irmb	Alzheimer's disease
Brenzavvy	Bexagliflozin	Type 2 diabetes
Jaypirca	Pirtobrutinib	GLP-1 for type 2 diabetes
Orserdu	Elacestrant	Breast cancer
Jesduvroq	Daprodustat	Anemia due to CKD
Lamzede	Velmanase alfa-tycv	Alpha-mannosidosis
Filspari	Sparsentan	Immunoglobin A nephropathy
Skyclarys	Omaveloxolone	Friedreich's ataxia

www.fda.gov

25

2023 Drug Approvals (2)

26

Brand	Generic	Description
Zavzpret	Zavegepant	Migraine
Daybue	Trofinetide	Rett syndrome
Zynyz	Retifanlimab-dlwr	Merkel cell carcinoma
Rezzayo	Resafungin	Candidemia
Joenja	Leniolisib	Phosphoinositide 3-kinase delta syndrome
Qalsody	Tofersen	Amyotrophic lateral sclerosis
Elfabrio	Pegunigalsidase alfa-iwxy	Fabry disease

www.fda.gov

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2023 Drug Approvals (3)

27

Brand	Generic	Description
Veozah	Fezolinetant	Menopausal hot flashes
Miebo	Perfluorhexyloctane	Dry eyes
Epkinly	Epcoritamab-bysp	Large B-cell lymphoma
Xacduro	Sulbactam/ Durlobactam	HAP, VAP
Paxlovid	Nirmatrelvir/ Ritonavir	COVID-19
Posluma	Flotufolastat F18	PET imaging prostate cancer
Inpefa	Sotagliflozin	Heart failure

www.fda.gov

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2023 Drug Approvals (4)

28

Brand	Generic	Description
Columvi	Glofitamab-gxbm	B-cell lymphoma
Litfulo	Ritlecitinib	Patchy hair loss
Rystiggo	Rozanolixizumab -noli	Myasthenia gravis
Ngenla	Somatrogon-ghla	Growth failure
Beyfortus	Nirsevimab-alip	RSV
Vanflyta	Quizartinib	Acute myeloid leukemia
Xdemvy	Lotilaner	Demodex blepharitis

www.fda.gov

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2023 New Formulations (1)

29

Brand	Generic	Description
Abilify Asimtufi	Aripiprazole	Extended release injectable for schizophrenia + bipolar
Airsupra	Albuterol/ Budesonide	New MDI for asthma
Atorvaliq	Atorvastatin	Oral suspension
Combgeisc	Acetaminophen/ Ibuprofen	Mild to moderate pain
Liqrev	Sildenafil	Oral suspension for PAH
Lumryz	Sodium oxybate	Extended-release powder for oral suspension
Mekinist	Trametinib	Metastatic melanoma

www.fda.gov

29

2023 New Formulations (2)

30

Brand	Generic	Description
Motpoly XR	Lacosamide	Extended-release capsule
Opvee	Nalmefene	Nasal spray
Prevduo	Neostigmine/ Glycopyrrolate	Fixed dose reversal of non-depolarizing NMBs
Rizafilm	Rizatriptan	Oral film
Rykindo	Risperidone	Long-acting injectable
Syfovre	Pegcetacoplan	Intravitreal injection
Symbicort Aerosphere	Budesonide/ Formoterol	New MDI for COPD
Tafinlar	Dabrafenib	Metastatic melanoma

www.fda.gov

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2023 New Formulations (3)

31

Brand	Generic	Description
Trikafta	Elexacaftor/ Tezacaftor/ Ivacaftor	Fixed dose combination for cystic fibrosis
Uzedy	Risperidone	Extended-release injection
Vevye	Cyclosporine	Ophthalmic solution for dry eyes
Zolpidem	Zolpidem	Immediate-release tablet

www.fda.gov

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Mavacamten (Camzyos)

32

- First-in-class cardiac myosin modulator indicated to improve functional capacity and symptoms in adults with NYHA class II or III obstructive hypertrophic cardiomyopathy (HCM)
- Adverse effects: dizziness (27%), syncope (6%)
- Boxed warning about risk of heart failure
- Dose is 5 mg PO daily, titrated to 15 mg/day
- One year cost is $89,500
- Can improve symptoms and may reduce the need for surgery in some patients with obstructive HCM that is refractory to standard pharmacologic treatment, but it can cause heart failure, interacts with many other drugs, and is very expensive
- Long-term data are needed

https://www.camzyos.com

32

Daridorexant (Quviviq)

33

- Treatment of sleep-onset insomnia and/or sleep-maintenance insomnia in adults
  - Suvorexant (Belsomra), Lemborexant (Dayvigo)
- Suppresses the wake drive by competitively inhibiting orexin A and B from binding to OX1R and OX2R
- Dosage is 25 or 50 mg once nightly $\leq$ 30 minutes before bedtime and $\geq$ 7 hours before planned awakening
- Side effects ($\geq$5%): headache, somnolence, fatigue
  - Excessive daytime sleepiness, sleep paralysis, hallucinations reported
- Use with strong CYP3A4 inhibitors or strong or moderate CYP3A4 inducers is not recommended; maximum dose with moderate CYP3A4 inhibitors is 25 mg
- Schedule IV controlled substance
- Modestly more effective than placebo, generally well-tolerated, no active-comparator trials

https://www.quviviq.com/

33

Terlipressin (Terlivaz)

34

- Vasopressin receptor agonist used to improve kidney function in adults with hepatorenal syndrome (HRS) with rapid reduction in kidney function
- Prodrug of lysine-vasopressin (antidiuretic hormone) binds to vasopressin I receptors in splanchnic circulation, reducing portal hypertension, increasing arterial volume and mean arterial pressure, and improving renal blood flow
- Approved for use outside of USA for more than 30 years
- Recommended by American College of Gastroenterology guidelines
- HRS complication of end-stage liver disease caused by hemodynamic changes related to portal hypertension that led to renal vasoconstriction and impairment
  - Typically managed with off-label use of albumin and either midodrine plus octreotide or norepinephrine

https://www.terlivaz.com

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Terlipressin (Terlivaz)

35

- Recommended Dosage Regimen (max treatment is 14 days)
  - Days 1 to 3 administer 0.85 mg (1 vial) intravenously every 6 hours
  - Day 4: Assess serum creatinine (SCr) versus baseline
    - If SCr ↓ by at least 30% from baseline, continue 0.85 mg IV every 6 hours
    - If SCr ↓ by less than 30% from baseline, dose may be increased to 1.7 mg IV every 6 hours
- Boxed Warning: SERIOUS OR FATAL RESPIRATORY FAILURE
- The most common adverse reactions (≥10%) include abdominal pain, nausea, respiratory failure, diarrhea, and dyspnea
- In a double-blind trial, addition of terlipressin to albumin reversed HRD more than the addition of placebo in patients with rapidly progressive kidney failure
- Terlipressin appears to be similar in efficacy to norepinephrine and more effective than midodrine plus octreotide

https://www.terlivaz.com

35

Treprostinol (Tyvaso DPI)

36

- Prostacyclin mimetic indicated for (PAH; WHO Group 1), (PH-ILD; WHO Group 3)
- Administer using a single inhalation per cartridge
- Administer in 4 separate treatment sessions each day approximately 4 hours apart, during waking hours
- Initial dosage: one 16 mcg cartridge per treatment session
  - Dosage should be increased by an additional 16 mcg per treatment session at approximately 1- to 2-week intervals, if tolerated
- Titrate to target maintenance doses of 48 mcg to 64 mcg per treatment session, 4 times daily

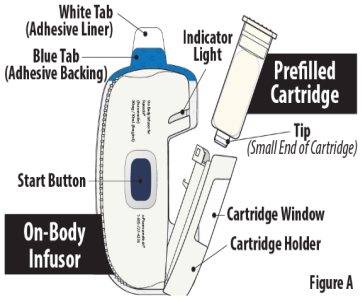
https://www.tyvasohcp.com/ph-ild/

36

Furosemide SC (Furoscix)

37

- SC loop diuretic administered via single-use, on-body infusor, for treatment of congestion due to fluid overload in NYHA Class II-III chronic heart failure
- Not for emergency situations or pulmonary edema
- Not for chronic use, patients should be switched to oral diuretic therapy as soon as practical
- Single-use infusor copackaged with 80 mg/10 mL pH neutral furosemide solution
- Approved based upon bioavailability
- Cost for one on-body infusor and prefilled cartridge is $822
  - Device programmed at 30 mg/hour, followed by 12.5 mg/hr x 4 hours



https://www.furoscix.com

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Dexmedetomidine (Igalmi)

38

- α-2 adrenergic receptor agonist indicated for the acute treatment of agitation associated with schizophrenia or bipolar I or II disorder in adults
- The safety and effectiveness has not been established beyond 24 hours from the first dose
- Administer sublingually or buccally - do not chew or swallow
- Adverse reactions (incidence ≥5% and at least twice the rate of placebo) are somnolence, oral paresthesia or oral hypoesthesia, dizziness, dry mouth, hypotension, and orthostatic hypotension
- Warning: hypotension, orthostatic hypotension, and bradycardia
- Drugs that prolong QT interval: avoid use

https://www.igalmihcp.com/igalmi-pi.pdf

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Dexmedetomidine (Igalmi) Dosing

39

Patient Population	Agitation Severity	Initial Dose*	Optional 2nd/3rd Doses*	Maximum Recommended Total Daily Dosage
Adults	Mild or Moderate	120 mcg	60 mcg	240 mcg
	Severe	180 mcg	90 mcg	360 mcg
Patients with Mild or Moderate Hepatic Impairment†	Mild or Moderate	90 mcg	60 mcg	210 mcg
	Severe	120 mcg	60 mcg	240 mcg
Patients with Severe Hepatic Impairment†	Mild or Moderate	60 mcg	60 mcg	180 mcg
	Severe	90 mcg	60 mcg	210 mcg
Geriatric Patients (≥ 65 years old)	Mild, Moderate, or Severe	120 mcg	60 mcg	240 mcg

https://www.igalmihcp.com/igalmi-pi.pdf

39

Tadalafil (Tadliq)

40

- PDE5 inhibitor indicated for the treatment of pulmonary arterial hypertension
- Oral Suspension: 20 mg/5 mL
- Dose is 40 mg (10 mL) once daily, with or without food
  - Use with ritonavir requires dosage adjustments
  - Dose adjustment with hepatic or renal dysfunction

https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/214522s000lbl.pdf

40

Sulbactam/Durlobactam (Xacduro)

41

- Indicated for hospital-acquired bacterial pneumonia (HABP) and ventilator-associated bacterial pneumonia (VABP) caused by susceptible strains of bacteria called *Acinetobacter baumannii-calcoaceticus* complex, for ≥ 18 years
- *Acinetobacter baumannii-calcoaceticus* complex (referred to as A. baumannii) includes four species of bacteria in the Acinetobacter family
  - Predominantly causes pneumonia, current treatments are limited
- Xacduro consists of sulbactam, a drug structurally related to penicillin, and durlobactam
  - Sulbactam kills *A. baumannii*
  - Durlobactam protects sulbactam from being degraded by enzymes that may be produced by *A. baumannii*

https://www.fda.gov/news-events/press-announcements/fda-approves-new-treatment-pneumonia-caused-certain-difficult-treat-bacteria

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Sulbactam/Durlobactam (Xacduro)

42

- Dose is (1 g of sulbactam, 1 g of durlobactam) every 6 hours by intravenous (IV) infusion over 3 hours in patients with creatinine clearance (CrCl) of 45 to 129 mL/min
- Dosing regimen adjustments are recommended for CrCl < 45 mL/min and CrCl ≥ to 130 mL/min
- Warning and precautions
  - Hypersensitivity reactions and *Clostridioides difficile*-associated diarrhea
- Adverse reactions (>10%): liver test abnormalities, diarrhea, anemia, and hypokalemia

https://xacduro-assets.s3.amazonaws.com/prescribing-information.pdf

42

Albuterol/Budesonide (Airsupra)

43

- Indicated for the as-needed treatment or prevention of bronchoconstriction and to reduce the risk of exacerbations in patients with asthma ≥ 18 years
- 180 mcg/160 mcg (administered as 2 puffs of albuterol/budesonide 90 mcg/80 mcg) by oral inhalation as needed for asthma symptoms
- Do not take more than 6 doses (12 inhalations) in a 24-hour period
- Adverse reactions (incidence ≥ 1%) are headache, oral candidiasis, cough, dysphonia

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Albuterol/Budesonide (Airsupra)

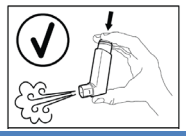
44

- Shake well before use?
  - Yes
- Priming
  - Before the first use: 4 sprays, if not used for more than 7 days or dropped: 2 sprays
- Cleaning
  - At least weekly
- Dose counter: Yes
- Beyond use date
  - 12 months after removal from foil pouch

www.astrazeneca.com

44

Budesonide/Formoterol (Symbicort Aerosphere)



45

- Approved April 2023 for COPD maintenance
- This is a new Symbicort formulation that uses the Aerosphere inhalation device
- Not indicated for the relief of acute bronchospasm or for the treatment of asthma
- The efficacy was established in two randomized, double-blind studies (TELOS and SOPHOS) in COPD
- Dose (total dose of budesonide 320 mcg/formoterol fumarate 9.6 mcg) twice daily by oral inhalation

https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/216579s000lbl.pdf

45

Sodium Oxybate (Lumryz)

46

- Extended-release oral suspension
  - Packets of 4.5 g, 6 g, 7.5 g, or 9 g
- Dosing
  - Initiate dosage at 4.5 g once per night orally
  - Titrate to effect in increments of 1.5 g per night at weekly intervals
  - Recommended range: 6 g to 9 g once per night orally
- Administration instructions
  - Prepare the dose prior to bedtime; suspend dose in approximately ⅓ cup of water in the mixing cup provided
  - Allow 2 hours after eating before dosing
  - Take dose while in bed and lie down after dosing

https://www.avadel.com/lumryz-prescribing-information.pdf

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Audience Question #4

47

- What is the recent approved dosage form for sildenafil (Liqrev) ?

- A. Injection
- B. Nasal spray
- C. Oral suspension
- D. Topical patch

47

Audience Question #5

48

- What is the maximum daily dose of albuterol/formoterol (Airsupra) ?

- A. 4 doses (8 inhalations)
- B. 6 doses (12 inhalations)
- C. 8 doses (16 inhalations)
- D. 12 doses (24 inhalations)

48

Audience Question #6

49

- What side effect is a concern for Terlipressin (Terlivaz) ?

- A. Administration site erythema
- B. Hallucinations
- C. Metabolic acidosis
- D. Respiratory failure

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The End

50

50