I Want a New Drug, New IV Medications FDA Approved 2023

Annemarie Hocking, PharmD

Clinical Pharmacist
PGY-1 Lead Preceptor
Option Care Health
Chicago Regional Compounding Center

1

Conflict of Interest:

No conflict of interest exists or needed to be resolved.

2

Objectives for Pharmacists

1. Recall clinical indications and mechanism of actions for select new medications approved by the US FDA in 2023
2. Describe dosing, administration and safety of new medications approved by the US FDA in 2023
3. Identify patient specific factors to appropriately assess, monitor and counsel patients receiving new mediations approved by the US FDA in 2023

3

Objectives for Technicians

1. Match new medications approved by the US FDA in 2023 with the conditions or diseases they are used to manage
2. Recognize the different characteristics, such as delivery systems, of new medications approved by the US FDA in 2023

4

Highlights

Brand Name	Generic Name	Category
Xacduro®	sulbactam/ durlobactam	Antibacterial
Rezzayo™	rezafungin	Antifungal
DefenCath™	taurolidine & heparin	Catheter lock solution
Vyjuvek™	beremagene geperpavec	Gene therapy biologic (topical)

5

Xacduro® (sulbactam/ durlobactam)

FDA approved
- May 23, 2023

Manufacturer
- INNOVIVA Specialty Therapeutics

Class
- Anti-infective

Indication
- Treatment of Hospital acquired, and ventilator associated bacterial pneumonia caused by Acinetobacter (HABP and VABP)

6

Xacduro® (sulbactam/ durlobactam)

- Acinetobacter resistance to Carbapenems and 3rd generation Cephalosporins
- Acinetobacter resistance is 5th most common cause of death attributed to drug resistance across the world (WHO)
- Mortality rate 26-55%

7

Xacduro® (sulbactam/ durlobactam)

- Sulbactam is beta-lactam antibacterial has bactericidal activity against A baumannii, and is a beta-lactamase inhibitor
- Durlobactam also is a beta-lactamase inhibitor that protects sulbactam from degradation by enzymes produced by A baumannii
- Durlobactam is the new novel drug

8

Xacduro® (sulbactam/ durlobactam)

Adverse Drug Reactions:	Approved for use in adults
• LFT abnormalities 19% • Diarrhea 17% • Anemia 13% • Hypokalemia 12% • Hypersensitivity reactions, • Infusion related reactions and C.Diff are also noted	• No data available for pediatrics or in pregnancy and lactation

9

Xacduro® (sulbactam/ durlobactam)

- "Copackaged Product" with sulbactam 1gm vial x1 and durlobactam 0.5gm vial x2
- NDC 68547-111-10 labeled by Lajolla Pharmaceutical Company
- Dosing:
  - Recommended dose is sulbactam 1gm/ durlobactam 1gm dependent on CrCl/ GFR adjusting frequency from every 4 hours to every 12 hours.
  - Total administration time: 3 hours

10

Xacduro® (sulbactam/ durlobactam)

- Preparation:
  - Reconstitute the sulbactam 1gm SDV with 5mL SWFI
    - Reconstituted product is not for direct patient infusion
  - Reconstitute each durlobactam 0.5gm SDV with 2.5mL SWFI
    - Reconstituted product is not for direct patient infusion
  - Withdraw 5mL of reconstituted sulbactam and 5mL (2.5 mL from 2 vials) of reconstituted durlobactam. Add the withdrawn volumes of both sulbactam and durlobactam to a 100 mL infusion bag of 0.9% Sodium Chloride for Injection, USP

11

Xacduro® (sulbactam/ durlobactam)

- Storage:
  - Store undiluted vials in refrigerator at 36-46 deg F
  - Store reconstituted and diluted medication in refrigerator at 36-46 deg F
- Stability
  - Medication is stable up to 24 hours after reconstitution
    - Stability includes length of infusion
  - Xacduro is only stable when reconstituted with SWFI, and diluted in NaCl 0.9%

12

Rezzayo™ (rezafungin)

FDA Approved:
- March 23, 2023

Manufacturer:
- Melinta Therapeutics

Class:
- Antifungal

Indication:
- Patients with limited treatment options for Candidemia and invasive Candidiasis

Not studied in Endocarditis, Osteomyelitis & Meningitis due to Candida

13

Rezzayo™ (rezafungin)

- Next generation Echinocandin showing better treatment for C albicans, C glabrata, C parapsilosis & C tropicalis
- Compliance – One IV infusion, once weekly, over 1 hour
- No apparent effect on QT interval prolongation

- Echinocandins work by inhibiting beta-d-glucan synthase enzyme. This enzyme is a major component of a fungal cell wall. By inhibiting this enzyme, fungal cell walls are damaged and destroyed.

14

Rezzayo™ (rezafungin)

Most common Adverse Drug Reactions (>5%):

- Hypokalemia, hypomagnesemia & hypophosphotemia
- Diarrhea, anemia, n/v, abdominal pain & constipation
- Infusion related side effects
- Photosensitivity
- Elevated Liver Function

Approved for use in adults

- No data available for pediatrics or in pregnancy and lactation

15

Rezzayo™ (rezafungin)

- Rezzayo 200mg sterile powder vial
- NDC 70842-240-01
- Dosing
  - 400mg IV loading dose week 1, followed by 200mg IV maintenance dose weekly for 3 additional doses
  - Safety >4 weeks not established
  - No adjustments for Renal or Hepatic insufficiency, or potential drug interactions

16

Rezzayo™ (rezafungin)

- Preparation:
  - For the 400 mg dose, reconstitute two 200mg vials each with 9.5 mL SWFI to provide a concentration of 20 mg/mL in each vial
  - For the 200 mg dose, reconstitute one 200mg vial with 9.5 mL SWFI to provide a concentration of 20 mg/mL.
    - Reconstituted product is not for direct patient infusion
  - Withdraw & discard the equal volume of drug dose from IV infusion bag (250mL NaCl 0.9%, NaCl 0.45% or D5W). Then add the total volume per dose to the infusion bag.

17

Rezzayo™ (rezafungin)

- Storage:
  - Store undiluted vials at 68-77 deg F
  - Store reconstituted solution at 41-77 deg F, stable upto 24 hours
  - Store diluted infusion medication at 41-77 def F, stable upto 48 hours
    - Stability includes length of infusion
- Rezzayo is only stable when reconstituted with SWFI, and diluted in NaCl 0.9%, NaCl 0.45% or Dextrose 5%

18

DefenCath™ (taurolidine & heparin)

FDA approval:
- November 15, 2023

Manufacturer:
- CorMedix

Class:
- Catheter lock solution

Indication:
- Reduce catheter related blood stream infections (CRBSI) in adult patients with kidney failure who receive hemodialysis (HD) via central venous catheters (CVC)

19

DefenCath™ (taurolidine & heparin)

- First, and only antimicrobial catheter lock solution US FDA approved
- Each year approx 250,000 CRBSI occur, with death occuring in approx 1/4 of these cases
- CRBSIs are caused by variety of pathogens, many that may be antibiotic resistant
- 80% of HD patients have CVC placed

20

DefenCath™ (taurolidine and heparin)

- Taurolidine
  - Derived from amino acid taurine
  - Gram +, Gram –, Mycobacteria and fungal coverage
  - Irreversible binding to cell walls leading to cell wall loss of integrity and cell death
  - Reduces bacterial stickiness to cells
  - Neutralizes bacterial endotoxins and exotoxins
- Heparin
  - Anticoagulant

21

DefenCath™ (taurolidine and heparin)

Warnings:	Adverse Drug Reactions:
• Heparin Induced Thrombocytopenia • Drug Hypersensitivity	• Nausea/ Vomiting (13%) • Bleeding (7%) • Dizziness (6%) • Musculoskeletal Chest Pain (3%)

22

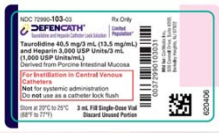
DefenCath™ (taurolidine and heparin)

- Dosing:
  - For instillation into CVC only
  - Not for systemic administration
  - Withdraw a sufficient volume from the DefenCath SDV to fill each catheter lumen. Instill catheter lock solution (CLS) into each catheter lumen at the conclusion of each HD session. Prior to start of the next HD session, aspirate CLS from the catheter and discard.

23

DefenCath™ (taurolidine and heparin)

- DefenCath
  - 3 mL SDV containing taurolidine 40.5 mg/3 mL and heparin 3,000 USP Units/3 mL - NDC 72990-103-03
  - 5 mL SDV containing taurolidine 67.5 mg/5 mL and heparin 5,000 USP Units/5 mL – NDC 72990-105-05
- Storage
  - Vials are to be kept at 68-77 deg F



24

Vyjuvek™ (beremagene geperpavec)

FDA Approval:
- May 19, 2023

Manufacturer:
- Krystal Biotech

Class:
- Gene Therapy Biologic

Indication:
- Topical gel used to treat wounds in patients with dystrophic epidermolysis bullosa (DEB) who are 6 months of age or older

25

Vyjuvek™ (beremagene geperpavec)

- DEB
  - Group of Genetic Blistering Disorders
  - Most common symptom is fragile skin – blistering, wounds, infection and scarring
  - Can also affect organs, and systems – GI, Urinary Tract, and Eyes
  - Mutation in Gene COL7A1 – responsible for making Type 7 Collagen. Type 7 Collagen is the primary component of anchoring fibrils which bind dermis to epidermis

26

Vyjuvek™ (beremagene geperpavec)

- Prior to Vyjuvek, treatment was primarily symptomatic
  - Medication for pain, and itching
  - Antibiotics
  - Symptomatic treatment (Blisters, Open wounds)
  - Skin grafting
  - Feeding tube
  - Physical Therapy/ Occupational Therapy

27

Vyjuvek™ (beremagene geperpavec)

- Delivers new COL7A1 genes directly to skin cells
- New COL7A1 in skin cells produces Type 7 Collagen
- Allows for Anchoring Fibrils to form and bind Dermis to Epidermis
- Total healing time 3-6 months
- Well tolerated
  - Side Effects include Itching and chills (both 10%), and Redness, Rash, Cough and Runny nose (all 6%)

28

Vyjuvek™ (beremagene geperpavec)

- Applied topically weekly by Healthcare Professional
- Ages 6 months – 3 years, weekly dose is 0.8 mL
- Ages > 3 years, weekly dose is 1.6 mL
- Apply droplets 1cm by 1cm apart into/ onto wound, then cover with water resistant dressing for first 24 hours. Continue to next wound and do the same until full dose used

29

Vyjuvek™ (beremagene geperpavec)

- Vials are stored in freezer at –13 – 5 deg F (through exp on vial), or refrigerator 36-46 deg F for 1 month
- Thaw Vyjuvek Biological Vial, & Excipient Gel Vial for 20 minutes prior to mixing
- Invert Vyjuvek Biological Vial 3-4 times, do not invert Excipient Gel Vial
- Withdraw 1 mL Vyjuvek & transfer into Excipient Gel Vial
- Remove air from mixed vial & shake vigorously
- Aseptically remove 0.4 mL dose from vial (x4 syringes total)

30

Vyjuvek™ (beremagene geperpavec)

- Vyjuvek administration syringes may be stored at room temperature (68 - 77 deg F) for up to 8 hours, and in the refrigerator (35.6 - 46.4 deg F) for up to 48 hours
- Discard all vials, supplies and used administration syringes in biohazard container
- Vyjuvek is a live, replication defective, herpes simplex virus type 1 vector gene therapy, specifically modified to express Type 7 Collagen
- Each carton of Vyjuvek (NDC 82194-510-02) contains one SDV of Vyjuvek biological suspension & one SDV of excipient gel. VYJUVEK biological suspension (inner NDC 82194-501-01) containing 5×109 PFU/mL. Excipient gel (inner NDC 82194-001-01) is supplied as a 1.5 mL fill volume in a separate single-use SDV

31

Questions?

- Thank you for your attendance

32

References:

- XACDURO® (sulbactam for injection; durlobactam for injection). www.xacduro.com. https://www.xacduro.com. Accessed February 3, 2024.
- Research C for DE and. FDA Approves New Treatment for Pneumonia Caused by Certain Difficult-to-Treat Bacteria. FDA. Published May 24, 2023. https://www.fda.gov/news-events/press-announcements/fda-approves-new-treatment-pneumonia-caused-certain-difficult-treat-bacteria. Accessed February 3, 2024.
- Home - Rezzayo. Published May 9, 2023. https://www.rezzayo.com/. Accessed February 3, 2024.
- *HIGHLIGHTS of PRESCRIBING INFORMATION*. https://www.rezzayo.com/wp-content/pdfs/REZZAYO%20(rezafungin%20for%20injection)%20Package%20Insert.pdf. Accessed February 3, 2024.
- Flanagan S, Goodman DB, Jandourek A, O'Reilly T, Sandison T. Lack of Effect of Rezafungin on QT/QTc Interval in Healthy Subjects. *Clinical Pharmacology in Drug Development*. 2019;9(4):456-465. doi:https://doi.org/10.1002/cpdd.757. Accessed February 3, 2024.
- *HIGHLIGHTS of PRESCRIBING INFORMATION*. https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/214520s000lbl.pdf. Accessed February 3, 2024.
- Once-Weekly Echinocandin Could Facilitate Continuity of Echinocandin Treatment and Outpatient Administration. ContagionLive. Published October 10, 2023. https://www.contagionlive.com/view/once-weekly-echinocandin-could-facilitate-continuity-of-echinocandin-treatment-and-outpatient-administration. Accessed February 3, 2024.
- About DefenCath™. CorMedix | Prevention of cardiac, renal and infectious diseases. https://cormedix.com/about-defencath/. Accessed February 3, 2024.
- *Disposal of Preparation Materials*. https://www.vyjuvekhcp.com/wp-content/uploads/pdf/vyjuvek-preparation-guide.pdf. Accessed February 3, 2024.
- Learn More About VYJUVEK® (beremagene geperpavec-svdt). VYJUVEK® (beremagene geperpavec-svdt) - Official Website. https://www.vyjuvek.com/about-vyjuvek/?pad_source=1&pclid=EAIaIQobChMIuZ-TrrO1hAMVfW5_AB3WmgDEAAYASAAEgKHAPD_BwE. Accessed February 3, 2024.
- *HIGHLIGHTS of PRESCRIBING INFORMATION VYJUVEK™ (Beremagene Geperpavec-Svdt) Biological Suspension Mixed with Excipient Gel for Topical Application Initial U.S. Approval: 2023 INDICATIONS and USAGE*. https://www.krystallabel.com/pdf/vyjuvek-us-pi.pdf. Accessed February 3, 2024.

33