NEW DRUG UPDATE
SUNDAY/8:00-9:30AM

ACPE UAN: 0107-9999-17-250-L01-P 0.15 CEU/1.5 hr
0107-9999-17-250-L01-T 0.15 CEU/1.5 hr

Activity Type: Application-Based

Learning Objectives for Pharmacists & Pharmacy Technicians:
Upon completion of this CPE activity participants should be able to:
1. Identify therapeutic indications of drugs recently approved by the FDA
2. Discuss the pharmacological properties of the new medications
3. List contraindications, warnings, precautions and significant drug interactions associated with each medication
4. Identify the normal dose and dosage forms of the drugs presented
5. Describe limitations to implementing the new medications into clinical practice

Speaker: Joe Strain, PharmD
Dr. Joe Strain is a clinical pharmacist residing in Rapid City, SD. He currently practices at Rapid City Regional Hospital where he has primarily worked with the hospitalist program since 2004. Joe also serves as Professor of Pharmacy Practice for the South Dakota State University College of Pharmacy. Joe received his Doctorate in Pharmacy from South Dakota State University and then completed a Pharmacy Practice Residency at the University of Utah Hospitals and Clinics in Salt Lake City, UT.

Speaker Disclosure: Joe Strain reports no actual or potential conflicts of interest in relation to this CPE activity. Off-label use of medications will not be discussed during this presentation.
Disclosure

• Joe Strain reports no actual or potential conflicts of interest associated with this presentation
Learning Objectives

• **Upon successful completion of this activity, participants should be able to:**
  - Identify therapeutic indications of drugs recently approved by the FDA.
  - Discuss pharmacological properties of the new medications.
  - List side effects, warnings, precautions and significant drug interactions associated with each medication.
  - Identify the normal dose and dosage forms of the drugs presented.
  - Describe limitations to implementing the new medications into clinical practice.

New Drug Approval Trends

Agenda

- Plecanatide (Trulance™)
- Naldemedine (Symproic®)
- Sofosbuvir/velpatasvir/voxilaprevir (Vosevi™)
- Glecaprevir/pibrentasvir (Mavyret™)
- Safinamide (Xadago®)
- Valbenazine (Ingrezza™)
- Delafloxacin (Baxdela™)
- Betrixaban (Bevyxxa®)
- Secnidazole (Solosec™)
- Herpes Zoster Vaccine (Shingrix®)
- Others

Which of the following is a contraindication to plecanatide?

<table>
<thead>
<tr>
<th>Condition</th>
<th>Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cancer</td>
<td>149414</td>
</tr>
<tr>
<td>Less than 6 years old</td>
<td>149424</td>
</tr>
<tr>
<td>Urinary tract infection</td>
<td>149425</td>
</tr>
<tr>
<td>Constipation</td>
<td>149426</td>
</tr>
</tbody>
</table>
Plecanatide (Trulance™)

- **Indications**
  - Chronic idiopathic constipation (CIC)

- **Pharmacology**
  - Uroguanylin analog
  - Stimulates guanylate cyclase type-C (GC-C) receptors → increases cGMP → activates CFTR → efflux of chloride from lining of GI tract leading to increased fluid secretion into intestinal lumen

- **Pharmacokinetics**
  - Not systemically absorbed
  - Metabolized to active metabolite in GI tract
  - Degraded into smaller peptides in the GI tract

- **Contraindications**
  - Bowel obstruction
  - Ages < 6 (due to risk of dehydration; mice data)

- **Warnings and precautions**
  - Ages 6-17
  - Diarrhea
### Diarrhea Reported from Phase III Trials

<table>
<thead>
<tr>
<th>Adverse reaction</th>
<th>Plecanatide N = 863</th>
<th>Placebo N = 870</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diarrhea</td>
<td>5%</td>
<td>1%</td>
</tr>
<tr>
<td>Severe diarrhea</td>
<td>0.6%</td>
<td>0.3%</td>
</tr>
<tr>
<td>Discontinued due to diarrhea</td>
<td>2%</td>
<td>0.5%</td>
</tr>
</tbody>
</table>

*Trulance PI 2017*

### Efficacy in Chronic Idiopathic Constipation

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Plecanatide 3 mg N = 453</th>
<th>Plecanatide 6 mg N = 441</th>
<th>Placebo N = 452</th>
</tr>
</thead>
<tbody>
<tr>
<td>*Response Rate</td>
<td>21%†</td>
<td>19.5%†</td>
<td>10.2%</td>
</tr>
<tr>
<td>First week responders</td>
<td>35.8%†</td>
<td>29.3%†</td>
<td>16.6%</td>
</tr>
<tr>
<td>CSBM within 24 hours</td>
<td>28.7%†</td>
<td>25.2%†</td>
<td>13.3%</td>
</tr>
</tbody>
</table>

*more than 3 complete spontaneous bowel movements (CSBM) per week, and increase of more than 1 CSBM/week in 9 of the 12 weeks

† p < 0.001 vs. placebo

Plecanatide (Trulance™)

- **Dosing**
  - 3 mg PO once daily with or without food
  - May be crushed and mixed in applesauce or water
- **Cost**
  - Plecanatide = $329.44 per month
  - Linaclotide = $329.38 per month

**Bottom line**
- Similar to linaclotide
- No data beyond 12 weeks
- Contraindicated in pediatric patients
- Likely for refractory cases of constipation
- Irritable bowel data pending

**Additional review**
**Naldemedine (Symproic®)**

- **Indication**
  - Opioid-induced constipation in chronic non-cancer pain

- **Pharmacology**
  - Structurally related to naltrexone
  - Side chain increases size & polarity
  - Decreases ability to penetrate blood-brain barrier
Naldemedine (Symproic®)

• Pharmacokinetics
  - T ½ ~ 11 hours
  - Primarily metabolized by CYP3A
  - Majority excreted via kidneys

• Contraindications
  - GI obstruction

Naldemedine (Symproic®)

• Warnings and precautions
  - GI perforation
  - Opioid withdrawal
  - No data in severe hepatic impairment

• Drug interactions
  - Avoid CYP3A inducers (e.g. carbamazepine, phenytoin, rifampin, St. John’s wort)
  - CYP3A inhibitors increase plasma levels (e.g. diltiazem, clarithromycin, fluconazole)
  - P-glycoprotein inhibitors increase plasma levels (e.g. amiodarone, verapamil)
## Adverse Reactions from 12-week Clinical Trials

<table>
<thead>
<tr>
<th>Reaction</th>
<th>Naldemedine N = 542</th>
<th>Placebo N = 546</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal pain</td>
<td>8%</td>
<td>2%</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>7%</td>
<td>2%</td>
</tr>
<tr>
<td>Nausea</td>
<td>4%</td>
<td>2%</td>
</tr>
<tr>
<td>Gastroenteritis</td>
<td>2%</td>
<td>1%</td>
</tr>
</tbody>
</table>

Symproic PI 2017

## Efficacy for Opioid Induced Constipation

<table>
<thead>
<tr>
<th></th>
<th>Naldemedine N = 273</th>
<th>Placebo N = 272</th>
<th>p-value (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Compose 1 Trial</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Response rate*</td>
<td>47.6</td>
<td>34.6</td>
<td>0.002 (4.8-21.3)</td>
</tr>
<tr>
<td>Compose 2 Trial</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Response rate*</td>
<td>52.5%</td>
<td>33.6%</td>
<td>&lt; 0.0001 (10.8-27)</td>
</tr>
</tbody>
</table>

*at least 3 SBMs/wk, and increase of at least 1 SBM/wk in 9 of the 12 weeks & 3 out of the last 4 weeks

Naldemedine (Symproic®)

- **Dosing**
  - 0.2 mg once daily with or without food

- **Cost**
  - #30 0.2 mg tablets = $350

- **Now available**
  - Was delayed likely due to being originally a Schedule II controlled substance
  - Descheduled on 9/29/2017

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Naldemedine (Symproic®)

- **Bottom line**
  - Another agent for opioid-induced constipation
  - Likely 2nd line after less expensive laxatives
  - No longer a C-II

- **Additional review**
**Sofosbuvir/velpatasvir/voxilaprevir (Vosevi™)**

- **Indication**
  - Treatment of hepatitis genotypes 1-6, previously treated with an NS5A inhibitor
  - Treatment of hepatitis genotypes 1a or 3 previously treated with sofosbuvir without an NS5A inhibitor

- **Pharmacology**
  - Block steps of viral replication
  - Sofosbuvir: HCV NS5B RNA polymerase inhibitor
  - Velpatasvir: HCV NS5A protein inhibitor
  - Voxilaprevir: NS3/4A protease inhibitor
### Pharmacokinetics

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Sofosbuvir</th>
<th>Velpatasvir</th>
<th>Voxilaprevir</th>
</tr>
</thead>
<tbody>
<tr>
<td>Effect of food on absorption</td>
<td>↑ 64-144%</td>
<td>↑ 40-166%</td>
<td>↑ 112-435%</td>
</tr>
<tr>
<td>T½</td>
<td>29h*</td>
<td>17h</td>
<td>33h</td>
</tr>
<tr>
<td>Urinary excretion</td>
<td>80%*</td>
<td>0.4%</td>
<td>0%</td>
</tr>
<tr>
<td>Metabolism</td>
<td>Cathepsin A</td>
<td>CYP2B6</td>
<td>CYP3A4</td>
</tr>
<tr>
<td></td>
<td>CES1</td>
<td>CYP2C8</td>
<td></td>
</tr>
<tr>
<td></td>
<td>HINT1</td>
<td>CYP3A4</td>
<td></td>
</tr>
</tbody>
</table>

* Active metabolite

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**Sofosbuvir/velpatasvir/voxilaprevir (Vosevi™)**

- **Contraindications**
  - Rifampin

- **Warnings/precautions**
  - Moderate to severe hepatic impairment
    - Child-Pugh B & C
  - Hepatitis B reactivation
  - Renal impairment (CrCl < 30 ml/min)
  - Drug interactions
    - Next slide
Sofosbuvir/velpatasvir/voxilaprevir (Vosevi™)

• Drug interactions
  - Many, many many…
  - Amiodarone—bradycardia
  - Avoid with P-gp inducers and moderate-potent CYP inducers
    • Reduces levels of all 3 agents
  - Avoid OATP inhibitors
    • Increases voxilaprevir
  - Acid-reducing drugs decrease velpatasvir absorption

### Common Adverse Reactions

<table>
<thead>
<tr>
<th></th>
<th>POLARIS-1</th>
<th></th>
<th>POLARIS-4</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Sof/Vel/Vox</td>
<td>Placebo</td>
<td>Sof/Vel/Vox</td>
<td>Placebo</td>
</tr>
<tr>
<td></td>
<td>N = 263</td>
<td>N = 152</td>
<td>N = 182</td>
<td>N = 151</td>
</tr>
<tr>
<td>Headache</td>
<td>21%</td>
<td>14%</td>
<td>23%</td>
<td>23%</td>
</tr>
<tr>
<td>Fatigue</td>
<td>17%</td>
<td>15%</td>
<td>19%</td>
<td>23%</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>13%</td>
<td>9%</td>
<td>14%</td>
<td>3%</td>
</tr>
<tr>
<td>Nausea</td>
<td>13%</td>
<td>7%</td>
<td>10%</td>
<td>3%</td>
</tr>
<tr>
<td>Insomnia</td>
<td>6%</td>
<td>3%</td>
<td>3%</td>
<td>1%</td>
</tr>
</tbody>
</table>

Sof/Vel/Vox = Sofosbuvir/velpatasvir/voxilaprevir
**POLARIS-1 Trial**

<table>
<thead>
<tr>
<th>GT</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>1a</td>
<td>101</td>
</tr>
<tr>
<td>1b</td>
<td>45</td>
</tr>
<tr>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>3</td>
<td>78</td>
</tr>
<tr>
<td>4</td>
<td>22</td>
</tr>
<tr>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>6</td>
<td>6</td>
</tr>
</tbody>
</table>

Sustained Virologic Response 12%

- GT-1a: 96%
- GT-1b: 100%
- GT-2: 100%
- GT-3: 95%
- GT-4: 91%
- GT-5: 100%
- GT-6: 100%

GT = genotype

**POLARIS-4 Trial**

<table>
<thead>
<tr>
<th>GT</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>1a</td>
<td>54</td>
</tr>
<tr>
<td>1b</td>
<td>44</td>
</tr>
<tr>
<td>2</td>
<td>24</td>
</tr>
<tr>
<td>3</td>
<td>22</td>
</tr>
</tbody>
</table>

Sustained Virologic Response 12%

- GT-1a: 98%
- GT-1b: 89%
- GT-2: 96%
- GT-3: 95%

GT = genotype

Sofosbuvir/velpatasvir/voxilaprevir (Vosevi™)

• Dosing
  - One tablet daily with food x 12 weeks
  - 400mg/100mg/100mg tablets

• Cost
  - $74,760 for 12 weeks

Sofosbuvir/velpatasvir/voxilaprevir (Vosevi™)

• Bottom line
  - First agent approved for those failing other new treatments
  - Convenient dosing
  - Expensive

• Additional review
  - http://www.hcvguidelines.org/
Glecaprevir/Pibrentasvir (Mavyret™)

- **Indication**
  - Hepatitis C genotypes 1-6, treatment naïve, may have mild cirrhosis
  - Hepatitis C genotype 1, previously failed an NS5A inhibitor OR an NS3/4A protease inhibitor

- **Pharmacology**
  - Glecaprevir: HCV NS3/4A protease inhibitor
  - Pibrentasvir: HCV NS5A inhibitor
Pharmacokinetics

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Glecaprevir</th>
<th>Pibrentasvir</th>
</tr>
</thead>
<tbody>
<tr>
<td>Effect of food on absorption*</td>
<td>↑ 83-163%</td>
<td>↑ 40-53%</td>
</tr>
<tr>
<td>T ½</td>
<td>6h</td>
<td>13h</td>
</tr>
<tr>
<td>Urinary excretion</td>
<td>0.7%</td>
<td>0%</td>
</tr>
<tr>
<td>Metabolism</td>
<td>CYP3A4 (secondary)</td>
<td>None</td>
</tr>
</tbody>
</table>

*moderate-high fat meal

Glecaprevir/Pibrentasvir (Mavyret™)

- **Contraindications**
  - Severe hepatic impairment (Child-Pugh C)
  - Rifampin and atazanavir
- **Warnings/precautions**
  - Moderate hepatic impairment (Child-Pugh B)
  - Hepatitis B reactivation
  - Carbamazepine, efavirenz, & St. John’s wort
Glecaprevir/Pibrentasvir (Mavyret™)

- Drug interactions
  - Both inhibit P-glycoprotein, BCRP and OATP
  - Both are substrates of P-gp and BCRP
  - Specific medication interactions listed in package insert
  - Specific list of medications NOT interacting listed in package insert

### Adverse Reactions from ENDURANCE-3 Trial

<table>
<thead>
<tr>
<th>Reaction</th>
<th>Glecaprevir/ Pibrentasvir 8 weeks N = 157</th>
<th>Glecaprevir/ Pibrentasvir 12 weeks N = 233</th>
<th>Daclatasvir/ sofosbuvir 12 weeks N = 115</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache</td>
<td>16%</td>
<td>17%</td>
<td>15%</td>
</tr>
<tr>
<td>Fatigue</td>
<td>11%</td>
<td>14%</td>
<td>12%</td>
</tr>
<tr>
<td>Nausea</td>
<td>9%</td>
<td>12%</td>
<td>12%</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>7%</td>
<td>3%</td>
<td>3%</td>
</tr>
<tr>
<td>Study (Genotype)</td>
<td>Population</td>
<td>SVR12</td>
<td>Treatment Duration</td>
</tr>
<tr>
<td>--------------------------</td>
<td>-------------------------------------------------</td>
<td>--------------</td>
<td>--------------------</td>
</tr>
<tr>
<td>ENDURANCE-4/SURVEYOR-1 (5, 6)</td>
<td>Treatment Naïve and IFN/RBV/Sof Experienced without cirrhosis</td>
<td>100% (57/57)</td>
<td>12 weeks</td>
</tr>
<tr>
<td>Surveyor-2 (2,4,5,6)</td>
<td>Treatment Naïve and IFN/RBV/Sof Experienced without cirrhosis</td>
<td>97% (248/255)</td>
<td>8 weeks</td>
</tr>
<tr>
<td>ENDURANCE-1 (1)</td>
<td>Treatment Naïve and IFN/RBV/Sof Experienced without cirrhosis</td>
<td>99% (348/351)</td>
<td>8 weeks</td>
</tr>
<tr>
<td>EXPEDITION-1 (1,2,4,5,6)</td>
<td>Treatment Naïve and IFN/RBV/Sof Experienced + cirrhosis</td>
<td>99% (145/146)</td>
<td>12 weeks</td>
</tr>
</tbody>
</table>

SVR12 = sustained virologic response at 12 weeks after end of treatment

ENDURANCE-3
(Treatment Naïve, Genotype 3, without cirrhosis)

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Glecaprevir/ Pibrentasvir 8 weeks N = 157</th>
<th>Glecaprevir/ Pibrentasvir 12 weeks N = 233</th>
<th>Daclatasvir/ sofosbuvir 12 weeks N = 115</th>
</tr>
</thead>
<tbody>
<tr>
<td>SVR12</td>
<td>94.9%</td>
<td>95.3%</td>
<td>96.5%</td>
</tr>
</tbody>
</table>

SVR12 = sustained virologic response at 12 weeks after end of treatment
Glecaprevir/Pibrentasvir (Mavyret™)

• Dosing
  - 100mg/40mg tablets
  - Take 3 tablets once daily with food
  - 4-week or 8-week supply
    • Wallets of 3 tablets each

• Cost
  - $26,400 for 8 weeks
  - $39,600 for 12 weeks

<table>
<thead>
<tr>
<th>HCV Genotype</th>
<th>Previous regimen</th>
<th>Treatment Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>NS5A inhibitor</td>
<td>16 weeks</td>
</tr>
<tr>
<td></td>
<td>NS3/4A protease inhibitor</td>
<td>12 weeks</td>
</tr>
<tr>
<td>1,2,4,5,6</td>
<td>Interferon, ribavirin or</td>
<td>8 weeks</td>
</tr>
<tr>
<td></td>
<td>sofosbuvir</td>
<td>12 weeks</td>
</tr>
</tbody>
</table>

Glecaprevir/Pibrentasvir Duration: Treatment Naïve Patients

<table>
<thead>
<tr>
<th>HCV Genotype</th>
<th>No cirrhosis</th>
<th>Child-Pugh A</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-6</td>
<td>8 weeks</td>
<td>12 weeks</td>
</tr>
</tbody>
</table>

Glecaprevir/Pibrentasvir Duration: Treatment-Experienced Patients

<table>
<thead>
<tr>
<th>HCV Genotype</th>
<th>Previous regimen</th>
<th>No cirrhosis</th>
<th>Child-Pugh A</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>NS5A inhibitor</td>
<td>16 weeks</td>
<td>16 weeks</td>
</tr>
<tr>
<td></td>
<td>NS3/4A protease inhibitor</td>
<td>12 weeks</td>
<td>12 weeks</td>
</tr>
<tr>
<td>1,2,4,5,6</td>
<td>Interferon, ribavirin or</td>
<td>8 weeks</td>
<td>12 weeks</td>
</tr>
<tr>
<td></td>
<td>sofosbuvir</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Glecaprevir/Pibrentasvir (Mavyret™)

• Bottom line
  - First 8-week treatment for all genotypes
  - Certain subtypes require 12 or 16 weeks
  - GT-1 patients failing previous treatment with new agents
  - Significantly cheaper list price vs. other approved treatments
  - May be used in renal failure

• Additional review
  - http://www.hcvguidelines.org/

Safinamide's mechanism is similar to which agent?

<table>
<thead>
<tr>
<th>Agent</th>
<th>Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rasagiline</td>
<td>150613</td>
</tr>
<tr>
<td>Pramipexole</td>
<td>150614</td>
</tr>
<tr>
<td>Levodopa</td>
<td>150615</td>
</tr>
<tr>
<td>Entacapone</td>
<td>150784</td>
</tr>
</tbody>
</table>
Safinamide (Xadago®)

• Indication
  - Add-on treatment for Parkinson’s disease
  - Reduces “off” episodes

• Pharmacology
  - Selective monoamine oxidase B inhibitor
  - Similar to rasagiline and selegiline
  - Also inhibits glutamate

Safinamide (Xadago®)

• Pharmacokinetics
  - Peaks in 2-3 hours
  - T ½ 20-26 hours
  - Steady-state in 5-6 days
  - Metabolized by 3 oxidative pathways (not CYP450 mediated)
    • Levels increased in hepatic impairment
      • Child Pugh B
  - Inactive metabolites excreted via kidneys
**Safinamide (Xadago®)**

**Contraindications**
- Hypersensitivity
- Severe hepatic impairment (Child-Pugh C)
- MAOI's (including linezolid)
- Meperidine, tramadol, methadone
- SNRIs, TCAs, cyclobenzaprine, methylphenidate, amphetamine derivatives, St. John’s Wort
- Dextromethorphan

**Warnings/precautions**
- Hypertension
- SSRI’s
- Sleep attacks
- Dyskinesia
- Psychosis/hallucinations
- Compulsive behaviors
- Withdrawal
- Retinal degeneration
Safinamide (Xadago®)

- Drug interactions
  - Increases levels of BCRP substrates (e.g. methotrexate, rosuvastatin)
  - Dopaminergic antagonists may decrease effectiveness
    - Antipsychotics
    - Metoclopramide

Adverse Reactions from Placebo-controlled Phase III Trials

<table>
<thead>
<tr>
<th>Reaction</th>
<th>Safinamide 50 mg N = 223</th>
<th>Safinamide 100 mg N = 498</th>
<th>Placebo N = 497</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dyskinesia</td>
<td>21%</td>
<td>17%</td>
<td>9%</td>
</tr>
<tr>
<td>Fall</td>
<td>4%</td>
<td>6%</td>
<td>4%</td>
</tr>
<tr>
<td>Nausea</td>
<td>3%</td>
<td>6%</td>
<td>4%</td>
</tr>
<tr>
<td>Insomnia</td>
<td>1%</td>
<td>4%</td>
<td>2%</td>
</tr>
<tr>
<td>Orthostatic hypotension</td>
<td>2%</td>
<td>2%</td>
<td>1%</td>
</tr>
</tbody>
</table>
### “On” Time Without Troublesome Dyskinesia

<table>
<thead>
<tr>
<th>Measurement (hours/day)</th>
<th>Safinamide 100 mg N = 274</th>
<th>Placebo N = 275</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>9.3</td>
<td>9.06</td>
</tr>
<tr>
<td>24 weeks</td>
<td>10.73</td>
<td>9.63</td>
</tr>
<tr>
<td>Change</td>
<td>+1.42</td>
<td>+0.57</td>
</tr>
<tr>
<td>Mean Difference from Placebo (95% CI)</td>
<td>+0.96 (0.56-1.37)*</td>
<td>NA</td>
</tr>
</tbody>
</table>


* P < 0.001

### “On” Time Without Troublesome Dyskinesia

<table>
<thead>
<tr>
<th>Measurement (hours/day)</th>
<th>Safinamide 50 mg N = 223</th>
<th>Safinamide 100 mg N = 224</th>
<th>Placebo N = 222</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>9.4</td>
<td>9.5</td>
<td>9.3</td>
</tr>
<tr>
<td>24 weeks</td>
<td>10.9</td>
<td>11</td>
<td>10.3</td>
</tr>
<tr>
<td>Change</td>
<td>1.5</td>
<td>1.5</td>
<td>1</td>
</tr>
<tr>
<td>Mean Difference from Placebo (95% CI)</td>
<td>0.51 (0.07-0.94)*</td>
<td>0.55 (0.12-0.99) †</td>
<td>NA</td>
</tr>
</tbody>
</table>


* p = 0.0223; † p = 0.013
Safinamide (Xadago®)

- Dosing
  - 50 mg daily for 2 weeks, then increase to 100 mg daily based on tolerability and response
  - Used with or without food
  - If stopping use 50 mg daily x 1 week
  - Max of 50 mg daily if moderate hepatic impairment

<table>
<thead>
<tr>
<th>MOA-B Inhibitors Monthly Cost Comparison</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Safinamide</td>
<td>Rasagiline</td>
</tr>
<tr>
<td>$670</td>
<td>$430</td>
</tr>
</tbody>
</table>

Safinamide (Xadago®)

- Bottom line
  - MAO-B inhibitor w/ glutamate inhibition
  - Likely use when not tolerating rasagiline or selegiline—no direct comparator trials
  - Must be used as add-on therapy (e.g. carbidopa/levodopa)

- Additional Review
  - Blair H. CNS Drugs 2017;31:169-76.
Valbenazine (Ingrezza™)

- **Indication**
  - Treatment of adults with tardive dyskinesia

- **Pharmacology**
  - Selectively inhibits vesicular monoamine transporter type 2 (VMAT-2)
  - VMAT is a protein in neurons that regulates storage of dopamine in neuronal vesicles
  - Inhibition of VMAT-2 results in reduction of synaptic dopamine levels
Valbenazine (Ingrezza™)

• Pharmacokinetics
  - Hydrolysis and CYP3A4 metabolism
    • Metabolite further metabolized by CYP2D6
  - Peaks in 0.5-1h (4-8 hours for active metabolite)
  - T ½ 15-22 hours
  - Steady-state in 1 week

Valbenazine (Ingrezza™)

• Contraindications
  - None listed

• Precautions/warnings
  - Somnolence
  - QT prolongation
    • Concern if on a strong CYP3A4 or CYP2D6 inhibitor, poor CYP2D6 metabolizer, or baseline QT prolongation
    • 11.7 msec vs 6.7 msec in poor CYP2D6 metabolizers
  - Not recommended in severe renal impairment
    • CrCl < 30 ml/min
Valbenazine (Ingrezza™)

- Drug interactions
  - Monoamine oxidase inhibitors
    - Concomitant use not recommended
  - Strong CYP3A4 inhibitors (e.g. itraconazole) & CYP2D6 inhibitors (e.g. fluoxetine)
    - Reduce dose
  - Strong CYP3A4 inducers (e.g. phenytoin)
    - Avoid use
  - May increase digoxin levels due to P-glycoprotein inhibition

**Adverse Reactions from 6-week placebo controlled trials**

<table>
<thead>
<tr>
<th>Reaction</th>
<th>Valbenazine N = 262</th>
<th>Placebo N = 183</th>
</tr>
</thead>
<tbody>
<tr>
<td>Somnolence</td>
<td>10.9%</td>
<td>4.2%</td>
</tr>
<tr>
<td>Anticholinergic effects</td>
<td>5.4%</td>
<td>4.9%</td>
</tr>
<tr>
<td>Falls/balance issues</td>
<td>4.1%</td>
<td>2.2%</td>
</tr>
<tr>
<td>Headache</td>
<td>3.4%</td>
<td>2.7%</td>
</tr>
<tr>
<td>Akathisia</td>
<td>2.7%</td>
<td>0.5%</td>
</tr>
<tr>
<td>Vomiting</td>
<td>2.6%</td>
<td>0.6%</td>
</tr>
<tr>
<td>Nausea</td>
<td>2.3%</td>
<td>2.1%</td>
</tr>
</tbody>
</table>
### KINECT 3 Trial Data

<table>
<thead>
<tr>
<th>Measure</th>
<th>Valbenazine 40mg N = 70</th>
<th>Valbenazine 80mg N = 79</th>
<th>Placebo N = 76</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline AIMS score</td>
<td>9.8</td>
<td>10.4</td>
<td>9.9</td>
</tr>
<tr>
<td>AIMS mean change at 6 weeks</td>
<td>-1.9</td>
<td>-3.2</td>
<td>-0.1</td>
</tr>
<tr>
<td>Placebo- difference (95% CI)</td>
<td>-1.8 (-3, -0.7) p &lt; 0.01</td>
<td>-3.1 (-4.2,-2.0) p &lt; 0.001</td>
<td>N/A</td>
</tr>
</tbody>
</table>


---

**Valbenazine (Ingrezza™)**

- **Dosing**
  - Initially 40 mg once daily with or without food
  - After 1 week increase to 80 mg once daily
  - Dose adjustments
    - Moderate to severe hepatic impairment (40mg daily)
    - CYP3A4 inhibitors (40 mg daily)
    - Poor CYP 2D6 metabolizers ("reduce dose")
    - CYP2D6 inhibitors ("reduce dose")

- **Cost**
  - #30, 40 mg capsules = $6330

Ingrezza PI 2017
Valbenazine (Ingrezza™)

• Bottom line
  - First agent approved for tardive dyskinesia
  - Benefit seen as soon as 2 weeks
  - Limited data up to 48 weeks
  - Somnolence most common side effect

• Additional review

Delafloxacin is a broad-spectrum fluoroquinolone antibiotic currently approved for pneumonia.

True 151600

False 151607
Delafloxacin (Baxdela™)

- Indication\(^1\)
  - Acute bacterial skin and skin structure infections
- Pharmacology\(^2\)
  - Fluoroquinolone antimicrobial
  - Lacks strong basic group at the C-7 position
  - “anionic” vs. “zwitterionic”
  - Increased activity in acidic environment

\(^1\)Baxdela PI 2017.

Delafloxacin (Baxdela™)

- Spectrum of activity
  - Gram-positive organisms
    - MSSA, MRSA, Streptococcus pyogenes, E. faecalis
  - Gram-negative organisms
    - E. coli, E. cloacae, K. pneumoniae, P. aeruginosa

Baxdela PI 2017.
Delafloxacin (Baxdela™)

- **Pharmacokinetics**
  - $T_{1/2} \sim 12$ hours
  - Oral bioavailability $\sim 59\%$
  - AUC of 450 mg PO similar to 300 mg IV
  - Metabolized primarily via glucuronidation
  - 65% renal elimination
    - Dose adjustments indicated

- **Contraindications**
  - Fluoroquinolone allergy

- **Warnings and precautions**
  - Similar to other fluoroquinolones
  - Tendon rupture, peripheral neuropathy, CNS effects
  - May exacerbate myasthenia gravis
  - *C. difficile*-associated diarrhea

- **Drug interactions**
  - Antacids, sucralfate, multivitamins

Baxdela PI 2017.
### Adverse Reactions from Phase 3 Clinical Trials

<table>
<thead>
<tr>
<th>Reaction</th>
<th>Delafloxacin N = 741</th>
<th>Vanco/aztreonam N = 751</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea</td>
<td>8%</td>
<td>6%</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>8%</td>
<td>3%</td>
</tr>
<tr>
<td>Headache</td>
<td>3%</td>
<td>6%</td>
</tr>
<tr>
<td>Increased transaminases</td>
<td>3%</td>
<td>4%</td>
</tr>
<tr>
<td>Vomiting</td>
<td>2%</td>
<td>2%</td>
</tr>
</tbody>
</table>

Baxdela PI 2017.

### Clinical Trial Data for Skin Infections

<table>
<thead>
<tr>
<th>Trial</th>
<th>Delafloxacin N =</th>
<th>Vancomycin/aztreonam N =</th>
<th>Treatment Difference (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PROCEED 1 Trial</td>
<td>331</td>
<td>329</td>
<td>-2.6 (-8.8, 3.6)</td>
</tr>
<tr>
<td>*Clinical Response rate</td>
<td>78.2%</td>
<td>80.9%</td>
<td></td>
</tr>
<tr>
<td>PROCEED 2 Trial</td>
<td>423</td>
<td>427</td>
<td>3.1 (-2.0, 8.3)</td>
</tr>
<tr>
<td>*Clinical Response rate</td>
<td>83.7%</td>
<td>80.6%</td>
<td></td>
</tr>
</tbody>
</table>

Baxdela PI 2017.
Delafloxacin (Baxdela™)

• Dosing
  - IV—300 mg every 12 hours over 60 minutes
  - PO—450 mg every 12 hours
  - Duration of 5-14 days
  - Give at least 2 hours before or 6 hours after antacids, sucralfate, metal cations
  - Give with or without food

• Renal impairment (CrCl 15-29 ml/min)
  - IV—200 mg every 12 hours; PO—No adjustment

• Avoid in end stage renal disease & dialysis
  - CrCl < 15 ml/min

Delafloxacin (Baxdela™)

• Bottom line
  - Unique fluoroquinolone for skin infections
  - MRSA activity
  - Similar warnings as other fluoroquinolones
  - Available both IV & PO

• Additional review
Betrixaban (Bevyxxa®)

• Indication
  - Prophylaxis of venous thromboembolism in hospitalized medical patients

• Pharmacology
  - Factor Xa inhibitor
Betrixaban (Bevyxxa®)

**Pharmacokinetics**
- Peaks in 3-4 hours
- Food decreases absorption for up to 6 hours after a meal
- T ½ 19-27 hours
- 85% GI, 11% renal elimination
- Minimal metabolism
- Renal impairment increases AUC 2-3x

Betrixaban (Bevyxxa®)

**Contraindications**
- Active bleeding

**Warnings/precautions**
- Spinal/epidural anesthesia
  - Wait 72 hours after last dose to remove epidural catheters
  - Wait 5 hours after catheter removal before giving next dose
- Severe renal impairment (CrCl 15-29 ml/min)
- Hepatic impairment

Betrixaban (Bevyxxa®)
Betrixaban (Bevyxxa®)

- Drug interactions
  - P-glycoprotein inhibitors
    - Amiodarone, azithromycin, verapamil
    - Requires dose reduction
  - Other anticoagulants/antiplatelets

<table>
<thead>
<tr>
<th>APEX Trial Cohort 1</th>
<th>Betrixaban N = 1914</th>
<th>Enoxaparin N = 1956</th>
<th>RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Composite</td>
<td>6.9%</td>
<td>8.5%</td>
<td>0.81 (0.65-1.00) p = 0.054</td>
</tr>
<tr>
<td>Asymptomatic DVT</td>
<td>5.5%</td>
<td>6.6%</td>
<td>NR</td>
</tr>
<tr>
<td>Symptomatic DVT</td>
<td>0.7%</td>
<td>0.1%</td>
<td>NR</td>
</tr>
<tr>
<td>Non-fatal PE</td>
<td>0.3%</td>
<td>0.9%</td>
<td>NR</td>
</tr>
<tr>
<td>VTE-related death</td>
<td>0.6%</td>
<td>0.6%</td>
<td>NR</td>
</tr>
<tr>
<td>Symptomatic events</td>
<td>1.3%</td>
<td>1.9%</td>
<td>0.67 (0.42-1.07) p = 0.09</td>
</tr>
</tbody>
</table>

### Overall Population

<table>
<thead>
<tr>
<th>Event</th>
<th>Betrixaban N = 3112</th>
<th>Enoxaparin N = 3174</th>
<th>RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Composite</strong>&lt;sup&gt;1&lt;/sup&gt;</td>
<td>5.3%</td>
<td>7%</td>
<td>0.76 (0.63-0.92)</td>
</tr>
<tr>
<td>Asymptomatic DVT</td>
<td>4.2%</td>
<td>5.5%</td>
<td>NR</td>
</tr>
<tr>
<td>Symptomatic DVT</td>
<td>0.4%</td>
<td>0.7%</td>
<td>NR</td>
</tr>
<tr>
<td>Non-fatal PE</td>
<td>0.3%</td>
<td>0.6%</td>
<td>NR</td>
</tr>
<tr>
<td>VTE-related death</td>
<td>0.4%</td>
<td>0.5%</td>
<td>NR</td>
</tr>
<tr>
<td><strong>Asymptomatic DVT</strong></td>
<td>4.2%</td>
<td>5.5%</td>
<td>NR</td>
</tr>
<tr>
<td><strong>Symptomatic DVT</strong></td>
<td>0.4%</td>
<td>0.7%</td>
<td>NR</td>
</tr>
<tr>
<td><strong>Non-fatal PE</strong></td>
<td>0.3%</td>
<td>0.6%</td>
<td>NR</td>
</tr>
<tr>
<td><strong>VTE-related death</strong></td>
<td>0.4%</td>
<td>0.5%</td>
<td>NR</td>
</tr>
<tr>
<td><strong>Symptomatic events</strong>&lt;sup&gt;1&lt;/sup&gt;</td>
<td>0.9%</td>
<td>1.5%</td>
<td>0.64 (0.42-0.98)</td>
</tr>
<tr>
<td><strong>Ischemic stroke</strong>&lt;sup&gt;2&lt;/sup&gt;</td>
<td>0.48%</td>
<td>0.91%</td>
<td>0.53 (0.3-0.94)</td>
</tr>
</tbody>
</table>

### Overall Safety Outcomes

<table>
<thead>
<tr>
<th>Event</th>
<th>Betrixaban N = 3716</th>
<th>Enoxaparin N = 3716</th>
<th>RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Major Bleeding</strong>&lt;sup&gt;1&lt;/sup&gt;</td>
<td>0.67%</td>
<td>0.57%</td>
<td>1.19 (0.67-2.12)</td>
</tr>
<tr>
<td>Gastrointestinal&lt;sup&gt;2&lt;/sup&gt;</td>
<td>0.51%</td>
<td>0.24%</td>
<td>NR</td>
</tr>
<tr>
<td>Intracranial hemorrhage&lt;sup&gt;2&lt;/sup&gt;</td>
<td>0.05%</td>
<td>0.19%</td>
<td>NR</td>
</tr>
<tr>
<td><strong>Fatal bleeding</strong>&lt;sup&gt;1&lt;/sup&gt;</td>
<td>0.03%</td>
<td>0.03%</td>
<td>NR</td>
</tr>
<tr>
<td><strong>Major or CRNM Bleeding</strong>&lt;sup&gt;1&lt;/sup&gt;</td>
<td>3.1%</td>
<td>1.6%</td>
<td>1.97 (1.44-2.68)</td>
</tr>
</tbody>
</table>

CRNM = clinically relevant non-major bleeding
Betrixaban (Bevyxxa®)

• Dosing
  - 160 mg x 1 then 80 mg once daily
  - Give with food
  - Duration of 35-42 days
  - If CrCl 15-29 ml/min
    • 80 mg x 1 then 40 mg once daily
  - Concomitant P-gp inhibitor
    • 80mg x 1 then 40 mg once daily

Betrixaban (Bevyxxa®)

• Availability & Cost
  - 40 mg and 80 mg capsules
  - ~ $18 per capsule or $630 for 35 days
**Betrixaban (Bevyxxa®)**

- **Bottom line**
  - First agent approved for extended prophylaxis in hospitalized medically ill patients
  - Use for 35-42 days
  - Watch for renal impairment and P-gp inhibitors
  - Potential to reduce ischemic stroke post hospitalization

- **Additional review**

---

**Secnidazole is approved for ___ day(s) of therapy.**

- One: **151680**
- Three: **151681**
- Seven: **151805**
- Ten: **151816**
Secnidazole (Solosec™)

- Indication
  - Bacterial vaginosis in adults

- Pharmacology
  - Nitroimidazole
  - Similar to metronidazole
  - Radial anions disrupt bacterial DNA leading to cell death

Secnidazole (Solosec™)

- Pharmacokinetics
  - Half-life ~ 17 hours
    - ~ 8 hours for metronidazole
  - Food does not affect kinetics
  - Metabolized by oxidation via CYP450 system
  - ~ 15% eliminated via renal system unchanged
Secnidazole (Solosec™)

• Contraindications
  - Nitroimidazole allergy

• Warnings and precautions
  - Vulvovaginal candidiasis
    • 9.6% vs. 2.9% placebo
  - Crosses placenta—no human data
  - Detected in breast milk—no human data
    • Recommended to pump and discard for 96 hours after administration

Secnidazole (Solosec™)

• Drug interactions
  - None noted
  - Warfarin?
    • Unknown
  - Alcohol?
    • One clinical trial did not allow alcohol (12 hours prior & for 3 days after administration)
    • In vitro studies show no effect on aldehyde dehydrogenase activity….but metronidazole hasn’t proven to inhibit it either...
    • Conservative approach is to avoid concomitant use

### Adverse Reactions Summary

|                          | Secnidazole  
|--------------------------|----------------------
|                          | N = 197              |
| Vulvovaginal candidiasis | 9.6%                 |
| Headache                 | 3.6%                 |
| Nausea                   | 3.6%                 |
| Diarrhea                 | 2.5%                 |
| Abdominal pain           | 2%                   |
|                          | Placebo N = 136      |
| Vulvovaginal candidiasis | 2.9%                 |
| Headache                 | 1.5%                 |
| Nausea                   | 0.7%                 |
| Diarrhea                 | 0.7%                 |
| Abdominal pain           | 1.5%                 |

*Source: PI 2017*

### Clinical Efficacy

<table>
<thead>
<tr>
<th></th>
<th>Secnidazole N= 243</th>
<th>Metronidazole N = 237</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall Therapeutic Success at Day 28 (mITT)</td>
<td>60.1%</td>
<td>59.5%</td>
<td>[-0.082, 0.094]</td>
</tr>
</tbody>
</table>

Secnidazole (Solosec™)

- **Dosing & administration**
  - 2 gram packet x 1 dose
  - With or without food
  - Sprinkle on applesauce, yogurt, pudding
  - Granules do not dissolve
  - Consume within 30 minutes
  - Do not chew granules
  - May follow with water

- **Bottom line**
  - First approved single dose treatment for bacterial vaginosis
  - Similar efficacy as metronidazole x 7 days
  - Similar adverse reaction profile as metronidazole
  - Monitor for candidiasis following treatment

- **Additional review**
Herpes Zoster Vaccine (Shingrix®)

- **Indication**
  - Prevention of herpes zoster in adults ≥ 50 years old
- **Pharmacology**
  - Varicella zoster virus glycoprotein E antigen
  - AS01B adjuvant to increase immune response
  - Non-live, recombinant vaccine
Herpes Zoster Vaccine (Shingrix®)

- **Contraindications**
  - Allergic reaction to Shingrix

- **Precautions/warnings**
  - Immunosuppressants *may* reduce efficacy
  - Trials on-going

### Adverse Reactions Overall Population—Pooled Data

<table>
<thead>
<tr>
<th>Reaction</th>
<th>Shingrix N = 4884</th>
<th>Placebo N = 4880</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain</td>
<td>78%</td>
<td>10.9%</td>
</tr>
<tr>
<td>Grade 3 pain</td>
<td>6.4%</td>
<td>0.37%</td>
</tr>
<tr>
<td>Redness</td>
<td>38.1%</td>
<td>1.3%</td>
</tr>
<tr>
<td>Swelling</td>
<td>26%</td>
<td>1%</td>
</tr>
<tr>
<td>Myalgia</td>
<td>44.6%</td>
<td>11.7%</td>
</tr>
<tr>
<td>Shivering</td>
<td>26.7%</td>
<td>5.8%</td>
</tr>
<tr>
<td>Fever</td>
<td>20.5%</td>
<td>3%</td>
</tr>
<tr>
<td>GI</td>
<td>17.3%</td>
<td>8.7%</td>
</tr>
</tbody>
</table>
### Efficacy with Shingrix vs. Placebo in ages ≥ 50 years

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Shingrix Herpes zoster cases</th>
<th>Placebo Herpes zoster cases</th>
<th>% Efficacy (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall population</td>
<td>6/7344</td>
<td>210/7415</td>
<td>97.2 (93.7, 99)</td>
</tr>
<tr>
<td>Ages 50-59</td>
<td>3/3492</td>
<td>87/3525</td>
<td>96.6 (89.6, 99.3)</td>
</tr>
<tr>
<td>Ages 60-69</td>
<td>2/2141</td>
<td>75/2166</td>
<td>97.4 (90.1, 99.7)</td>
</tr>
<tr>
<td>Ages ≥ 70</td>
<td>1/1711</td>
<td>48/1724</td>
<td>97.9 (87.9, 100)</td>
</tr>
</tbody>
</table>


### Efficacy with Shingrix vs. Placebo in ages ≥ 70 years

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Shingrix herpes zoster cases</th>
<th>Placebo herpes zoster cases</th>
<th>% Efficacy (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>23/6541</td>
<td>223/6622</td>
<td>89.8 (84.2, 93.7)</td>
</tr>
<tr>
<td>Ages 70-79</td>
<td>17/5114</td>
<td>169/5189</td>
<td>90.0 (83.5, 94.4)</td>
</tr>
<tr>
<td>Ages ≥ 80</td>
<td>6/1427</td>
<td>54/1433</td>
<td>89.1 (74.6, 96.2)</td>
</tr>
</tbody>
</table>

Herpes Zoster Vaccine (Shingrix®)

• Dose
  - Two IM injections (0.5ml) separated by 2 to 6 months
  - Deltoid region of upper arm
  - Reconstitute lyophilized antigen vial with adjuvant suspension diluent prior to administration (stable for 6 hours if refrigerated)
  - Preservative free

• Storage
  - Both vials in refrigerator

Herpes Zoster Vaccine (Shingrix®)

• ACIP Recommendations
  - Shingrix recommended for immunocompetent adults aged > 50
  - Includes those who previously received Zostavax
    • As early as 8 weeks after receiving Zostavax
  - Shingrix is preferred over Zostavax
    • Greater protection especially among elderly

Herpes Zoster Vaccine (Shingrix®)

- **Bottom line**
  - Improved efficacy rates over Zostavax®
  - 2 shot IM series separate by 2-6 months
  - Store in refrigerator
  - Pain and other reactions are common but majority not severe

- **Additional review**
  - Shingles Vaccine: FAQs. Pharmacists Letter 2017; resource #331201.
**Glycopyrrolate (Lonhala™ Magnair®)**

- **Indication**
  - Long acting muscarinic antagonist for long-term maintenance of chronic obstructive pulmonary disease (COPD)
  - First long-acting agent in nebulized formulation

- **Dosing**
  - 25 mcg (1ml) twice daily nebulized

- Only use with Magnair nebulizer
Glycopyrrolate (Lonhala™ Magnair®)

**Administration**
- Remove vial from foil pouch immediately prior to use
- Insert vial into medication cap
- When medication cap is attached to inhaler the vial is punctured
- Treatment takes ~ 2-3 minutes
- Must wash components after each use
- Components replaced every 30 days.


Glycopyrrolate (Lonhala™ Magnair®)

**Bottom line**
- First long acting muscarinic antagonist for COPD available as a nebulizer
- Alternative to inhalers
- Wash components after every use
- Expected availability Spring 2018

**Additional review**
**Meropenem/Vaborbactam (Vabomere™)**

- **Indication**
  - Complicated urinary tract infections

- **Pharmacology**
  - Carbapenem plus new beta-lactamase inhibitor
  - Effective against KPC producing organisms
  - Does not inhibit all carbapenemase classes

- **Bottom line**
  - Welcomed addition against carbapenemase producing bacteria

**Ozenoxacin (Xepi™)**

- **Indication**
  - Topical cream for impetigo due to *Staphylococcus aureus* or Streptococcal pyogenes (ages ≥ 2 months)

- **Pharmacology**
  - Quinolone

- **Dosing**
  - Apply thin layer twice daily for 5 days

- **Alternative topical agent to mupirocin or retapamulin**
Questions?