Updates in Drug Therapy

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Objectives

For select medications approved in the previous 12 months, the attendee will be able to:

• Discuss mechanisms of action, dosing, adverse effects, and monitoring
• Review pertinent indications and contraindications for therapy
• Identify patients who would benefit from treatment with new medications
Conflicts of Interest

- I have no actual or potential conflict of interest in relation to this program.
Abbreviations

- ASCVD: atherosclerotic cardiovascular disease
- CVD: cardiovascular disease
- GP IIb/IIIa: glycoprotein IIb/IIIa
- HLD: hyperlipidemia
- LDL-c: low-density lipoprotein cholesterol
- LMWH: low molecular weight heparin
- MI: myocardial infarction
- NVAF: non-valvular atrial fibrillation
- OAT4: organic anion transporter 4
- PCI: percutaneous coronary intervention
- PCSK-9: Proprotein convertase subtilisin/kexin type 9
- TSOAC: target-specific oral anticoagulant
- UFH: unfractionated heparin
- URAT1: uric acid transporter 1
- URTI: upper respiratory tract infection
- VTE: venous thromboembolism
Select Resources for Newly Approved Medications

- www.fda.gov.cder
- Facts and Comparisons
- The Medical Letter
- The Pharmacist’s Letter
- www.lexi.com
- Micromedex Drugdex™
- APhA New Drug Bulletins
Approvals in 2015

- 45 novel agents approved
  - Historical previous 10 year average = 28
  - Highest approval number in 19 years
- 31% were fast track
  - Medications with potential to address unmet needs
- 47% were orphan drugs
  - Diseases that affect ≤200,000 Americans
- 36% were approved as the first drug within a pharmacologic class
Newly Approved Medications

- Cardiology
- Endocrinology
- Miscellaneous
Cardiology
Cardiovascular Disease (CVD)

- CVD is the leading cause of death for men and women
  - >375,000 deaths/year

- Lifetime Risk after age of 40
  - Men: 49%
  - Women: 32%

- Coronary heart disease (CHD) comprises more than half of the CVD events
Proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors

- PCSK9 binds to LDL receptor (LDLRs) on hepatocyte surface
  - Promote LDLR degradation within liver
  - Results in higher circulating LDL-c
- PCSK9 inhibitors increase LDLRs
  - Reduce circulating LDL-c
- When added to statin therapy:
  - Lower LDL 30%-70%
  - Lower TG 12%-17%
  - Increase HDL 4%-7%
- Outcomes studies: post hoc/exploratory analyses have demonstrated reduction in CV events

<table>
<thead>
<tr>
<th>Medication</th>
<th>Alirocumab (Praluent™)</th>
<th>Evolocumab (Repatha™)</th>
</tr>
</thead>
</table>
| **Indication** | • Adjunct to diet and maximally tolerated statin therapy  
• Treatment of adults with heterozygous familial hypercholesterolemia (HeFH) or clinical ASCVD who require additional lowering of LDL-c |
| **Dosage and Administration** | • 75 mg SC once every 2 weeks  
• Can titrate to 150 mg SC once every 2 weeks after 4-8 weeks if needed  
• No renal or hepatic dose adjustment | • HeFH: 140 mg SC once every 2 weeks  
OR 420 mg SC once every month  
• HoFH: 420 mg SC once every month  
• Primary HLD with established ASCVD: 140 mg SC once every 2 weeks  
OR 420 mg SC once every month  
• No renal or hepatic dose adjustment |
| **Adverse Effects (≥5%)** | Nashopharyngitis, injection site reactions, influenza | Nashopharyngitis, injection site reactions, influenza, URTI, back pain |
| **Contraindications** | | Hypersensitivity reaction |
| **Monitoring** | Lipid panel | |
| **Cost** | ~$1100-1300 | |
AB is a 67 year old male with a past medical history of dyslipidemia, non-ST segment myocardial infarction (NSTEMI), and hypertension. He states that he has been able to tolerate multiple statins in the past.

Fasting lipid panel (2 days prior)
TC 260 mg/dL  HDL 36 mg/dL  TG 250 mg/dL  LDL 174 mg/dL
All other labs within normal limits

Which of the following medications and doses would be appropriate for AB?

a. Alirocumab (Praluent™) 75 mg SC twice monthly
b. Alirocumab (Praluent™) 150 mg SC once monthly
c. Evolocumab (Repatha™) 140 mg SC once monthly
d. Patient does not have an indication for this class of medications
Cangrelor (Kengreal™)

• Indication
  ▫ Adjunct to PCI for reducing risk of periprocedural MI, repeat coronary revascularization, and stent thrombosis
  ▫ For patients who have NOT been treated with a P2Y12 platelet inhibitor and are not being given a GP IIb/IIIa inhibitor

• MOA
  ▫ Selectively and reversibly to P2Y12 receptors to block ADP-induced platelet activation and aggregation
Cangrelor (Kengreal™)

- **Dosage and administration**
  - 30 mcg/kg IV bolus prior to PCI followed by a 4 mcg/kg/min IV infusion for at least 2 hours or duration of procedure, whichever is longer.

- **Adverse effects**
  - Bleeding

- **Contraindications**
  - Significant active bleeding
  - Hypersensitivity
  - Clopidogrel and prasugrel should not be given during infusion

- **Cost:** ~$750/vial
  - Patients weighing >100 kg need 2 vials
  - Manufacturer will accept outdated or unused vials.
Edoxaban (Savaysa™)

- **Indication**
  - Reduce risk of stroke and systemic embolism in patients with non-valvular atrial fibrillation
  - Treatment of VTE following 5-10 days of initial therapy with parenteral anticoagulant

- **MOA:** selective inhibitor of Factor Xa

- **Dosage and administration**
  - **NVAF:**
    - CrCL >50 to ≤95 mL/min: 60 mg once daily
    - CrCL 15 to 50 mL/min: 30 mg once daily
  - **VTE:**
    - 60 mg once daily
    - 30 mg once daily
    - CrCL 15 to 50 mL/min
    - ≤60 kg
    - P-gp inhibitors

Savaysa (edoxaban) [prescribing information].
# Edoxaban (Savaysa™)

<table>
<thead>
<tr>
<th>From*</th>
<th>To</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Warfarin</td>
<td>Edoxaban</td>
<td>Discontinue warfarin. Start edoxaban when INR is ≤2.5</td>
</tr>
<tr>
<td>TSOAC</td>
<td>Edoxaban</td>
<td>Discontinue oral anticoagulant. Start edoxaban at time of next scheduled dose</td>
</tr>
<tr>
<td>LMWH</td>
<td>Edoxaban</td>
<td>Discontinue LMWH. Start edoxaban at time of next scheduled administration of LMWH</td>
</tr>
<tr>
<td>UFH</td>
<td>Edoxaban</td>
<td>Discontinue infusion. Start edoxaban 4 hours later</td>
</tr>
</tbody>
</table>

*Refer to PI for instructions regarding transitioning from edoxaban to other anticoagulants

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*Savaysa (edoxaban) (prescribing information).*
Edoxaban (Savaysa™)

- **Contraindications**
  - Active bleeding
  - Do not use in patients with CrCl > 95 mL/min
  - Not recommended with moderate-severe hepatic impairment (Child-Pugh B and C)

- **Monitoring:** renal function

- **Cost:** ~$350 for 30 day supply

- **Adverse effects**
  - AF: ≥5%
    - Bleeding
    - Anemia
  - VTE: ≥ 1%
    - Bleeding, anemia
    - Rash
    - Abnormal LFTs
# FDA Approvals of TSOAC

<table>
<thead>
<tr>
<th>Panel</th>
<th>Edoxaban (Savaysa)</th>
<th>Dabigatran (Pradaxa)</th>
<th>Rivaroxaban (Xarelto)</th>
<th>Apixaban (Eliquis)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stroke and systemic thromboembolism prevention in atrial fibrillation</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>DVT prophylaxis in orthopedic surgery</td>
<td>Approved in Japan</td>
<td>Approved in Europe and Canada</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>DVT prophylaxis in hospitalized medical patients</td>
<td></td>
<td></td>
<td>Higher bleeding than enoxaparin; no FDA application</td>
<td></td>
</tr>
<tr>
<td>VTE acute treatment and secondary prevention</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>ACS: CV death, MI, or stroke prevention</td>
<td></td>
<td></td>
<td>Rejected by FDA</td>
<td>Trial stopped early for excess bleeding</td>
</tr>
</tbody>
</table>

Adapted from: ACCP 2016 Updates in Therapeutics. Cardiology I.
Idarucizumab (Praxbind®)

- **Indication**
  - For patients treated with dabigatran (Pradaxa) when anticoagulation reversal is needed
    - Emergency surgery/urgent procedures
    - Life-threatening/uncontrolled bleeding

- **MOA**
  - Humanized monoclonal antibody fragment (Fab)
    - Binds to dabigatran and metabolites

- **Dosage and administration**
  - 5 grams IV
    - Provided as 2 separate vials containing 2.5g/50 mL idarucizumab
    - Can administer as 2 consecutive infusions or bolus injection
Idarucizumab (Praxbind™)

- **Adverse effects (≥5%):**
  - Hypokalemia
  - Delirium
  - Constipation
  - Pyrexia
  - Pneumonia
- **Contraindications:** none
  - **Warnings & precautions:**
    - Thromboembolic risk
    - Hypersensitivity reactions
    - Risk of serious ADRs in patients with hereditary fructose intolerance

- **Monitoring**
  - Re-elevation of coagulation parameters
    - Dabigatran overdose
      - Baseline aPTT, repeat 2 hours postexposure, every 12 hours until aPTT returns to normal
  - Signs/symptoms of clinically relevant bleeding
  - Thromboembolic risk
    - Can restart dabigatran 24 hours after administration

- **Cost**
  - $4200/2 vials
REVERSE-AD

- 123 patients
  - Bleeding: n=66
  - Need for procedure: n=57
- Interim analysis of 90 patients
- Median maximum percentage reversal: 100%
- Median time to bleeding cessation: 11.4 hours
- Normal hemostasis reported in 92% of patients undergoing surgery
- Thrombotic events: 5
- Deaths reported: 18 (9 in each group)
  - Appeared to be related to index event

Which of the following patients would be a candidate for treatment with edoxaban (Savaysa™)?

a. A 65 year old patient undergoing orthopedic surgery
b. A 70 year old patient with a history of non-valvular atrial fibrillation
c. A 68 year old patient hospitalized for pneumonia
d. An 80 year old patient hospitalized for acute coronary syndrome
Sacubitril/valsartan (Entresto™)

- Indication
  - Reduce the risk of cardiovascular death and hospitalization for heart failure in patients with chronic heart failure (NYHA Class II-IV) and reduced ejection fraction (HFrEF)
  - Used in place of ACEi or ARB

- Dosage and administration
  - 49/51 mg (sacubitril/valsartan) PO twice-daily
  - Double the dose after 2-4 weeks to target maintenance dose of 97/103 mg twice daily
  - Reduce the starting dose to 24/26 mg twice daily for:
    - Patients not currently taking ACEi or ARB or previously taking low dose of these agents
    - Severe renal impairment (eGFR<30 mL/min/1.73 m²)
    - Moderate hepatic impairment (Child-Pugh B)
Sacubitril/valsartan (Entresto®)

- Adverse effects (≥5%)
  - Hypotension
  - Hyperkalemia
  - Cough
  - Dizziness
  - Renal failure
- Cost
  - $7.50/tablet
  - $450 (60 count)
  - $750 (100 count)
  - $1125 (180 count)
- Contraindications
  - Hypersensitivity
  - Angioedema related to ACEi or ARB
  - Concomitant use of ACEi or ARB
    - Do not administer within 36 hours of ACEi
  - Concomitant use of aliskiren in patients with diabetes
- Monitoring
  - Renal function
  - Potassium
  - s/s angioedema/hypotension
  - Improvement in s/s HF

Entresto (sacubitril and valsartan) [prescribing information].
### Population (n=8442)

**Inclusion**
- NYHA Class II-IV
- EF ≤40%
- BNP 100-150 pg/mL
- Stable dose of BB, ACEi, ARB

**Exclusion**
- Symptomatic hypotension
- SBP<100 mm Hg
- eGFR<30 ml/min/1.73m²
- Potassium >5.2 mmol/L
- h/o angioedema

### Intervention

- **Entresto 200 mg BID + standard of care**
- **Enalapril 10 mg BID + standard of care**

### Efficacy Results

**Primary Outcome:** (composite of death from cardiovascular causes or a first hospitalization for heart failure)
- HR = 0.80 (0.73-0.87)
- P = 0.0000004
- NNT = 21

**CV death**
- HR = 0.80 (0.71-0.89)
- P < 0.001

**All-cause mortality**
- HR = 0.84 (0.76-0.93)

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*PARADIGM-HF*

Ivabradine (Corlanor®)

- **Indication**
  - To reduce the risk of hospitalization for worsening HF in patients with stable, symptomatic, chronic HF
    - LVEF ≤35%
    - Sinus rhythm with resting HR ≥70 bpm
    - Either on maximally tolerated BB dose or CI to BB

- **MOA**
  - Blocks hyperpolarization-activated cyclic nucleotide-gated (HCN) channel in sinoatrial node, responsible for \( I_f \) current
    - Delays diastolic depolarization, reduces HR
  - Does not affect other ion channels
  - Does not alter myocardial contractility or intra-cardiac conduction
Ivabradine (Corlanor®)

• Dosage and administration
  ▫ 5 mg BID
    • Can adjust dose after 2 weeks based on HR up to 7.5 mg BID
    • Resting HR 50-60 bpm
  ▫ 2.5 mg BID
    • Patients with conduction defects
    • Bradycardia could lead to hemodynamic compromise

• Contraindications
  ▫ Acute decompensated HF
  ▫ BP <90/50 mm Hg
  ▫ Sick sinus syndrome, sinoatrial block or 3rd degree AV block
    • Unless functioning pacemaker
  ▫ Resting HR <60 bpm prior to treatment
  ▫ Severe hepatic impairment (Child-Pugh C)
  ▫ Pacemaker dependence
    • HR maintained exclusively by pacemaker
  ▫ Strong CYP3A4 inhibitors

• Adverse effects (≥1%)
  ▫ Bradycardia
  ▫ Hypertension
  ▫ Atrial fibrillation
  ▫ Luminous phenomena (phosphenes)

• Cost
  ▫ $468/60 tablets
  ▫ $1404/180 tablets
## SHIFT

**Population (n=6558)** | **Intervention** | **Efficacy Results**
---|---|---
**Inclusion**
NYHA Class II-IV  
EF ≤35%  
HR ≥70 bpm  
Admitted to hospital for HR within previous year  
On stable background treatment, including BB

<table>
<thead>
<tr>
<th>Ivabradine 7.5 mg BID + standard of care</th>
</tr>
</thead>
</table>

**Exclusion**

Recent MI
Ventricular or atrioventricular pacing that is operative >40% of the time
Atrial fibrillation
Symptomatic hypotension

<table>
<thead>
<tr>
<th>Placebo + standard of care</th>
</tr>
</thead>
</table>

**Primary Outcome:**
(Composite of cardiovascular death or hospital admission for worsening heart failure)

HR = 0.82 (0.75-0.90)  
P < 0.0001

CV death

HR = 0.91 (0.80-1.03)  
P < 0.0001

HF hospitalization

HR = 0.74 (0.66-0.83)  
P < 0.0001
TW is a 74 year old female who presents with HFrEF, NYHA III. Her past medical history is significant for hypertension, dyslipidemia, and peripheral arterial disease. She is currently taking carvediolol 25 mg BID, spironolactone 25 mg daily, furosemide 80 mg BID, potassium chloride 20 mEq BID, aspirin 81 mg daily, and atorvastatin 80 mg daily. She has been hospitalized twice in the past year for HF exacerbation. She states that her symptoms have been stable over the past 3 months. Allergies include lisinopril (angioedema).

Vitals: BP 150/90 mm Hg   P 80 bpm   Wt 185 lbs   Ht 5’7’’   EF 35%

Which medication would be most appropriate for TW at this visit?

a. Edoxaban (Savaysa™) 60 mg once daily
b. Sacubitril/valsartan (Entresto™) 24/26 mg twice daily
c. Ivabradine (Corlanor®) 5 mg twice daily
d. None of these medications are appropriate for this patient
Endocrinology
Insulin degludec injection (Tresiba®)

• Indication
  ▫ Ultra long-acting human insulin analog indicated to improve glycemic control in adults with diabetes mellitus

• Dosing and administration
  ▫ Available via FlexTouch pens
  ▫ Dose once daily based on metabolic needs
  ▫ Recommended to wait 3-4 days between dose increase
  ▫ Unit-to-unit conversion from other long-acting insulins

<table>
<thead>
<tr>
<th>Tresiba</th>
<th>Total Volume</th>
<th>Conc.</th>
<th>Total Units</th>
<th>Max Dose per Injection</th>
<th>Dose Increment</th>
<th>Package Size</th>
</tr>
</thead>
<tbody>
<tr>
<td>U-100</td>
<td>3 mL</td>
<td>100 units/mL</td>
<td>300</td>
<td>80 units</td>
<td>1 unit</td>
<td>5 pens/pack</td>
</tr>
<tr>
<td>U-200</td>
<td>3 mL</td>
<td>200 units/mL</td>
<td>600</td>
<td>160 units</td>
<td>2 units</td>
<td>3 pens/pack</td>
</tr>
</tbody>
</table>
## Comparison of Basal Insulin Therapy

<table>
<thead>
<tr>
<th>Preparation</th>
<th>Onset</th>
<th>Peak</th>
<th>Half-life</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Detemir</td>
<td>1-1.5 hr</td>
<td>4-7 hr (peak not pronounced)</td>
<td>5-7 hr</td>
<td>14 – 24 hr</td>
</tr>
<tr>
<td>Glargine 100 unit/ml</td>
<td>1-1.5 hr</td>
<td>8-12 hr (peak not pronounced)</td>
<td>12 hr</td>
<td>Up to 24 hr</td>
</tr>
<tr>
<td>Glargine 300 unit/ml</td>
<td>2 hr</td>
<td>Close to peakless</td>
<td>19 hr</td>
<td>32</td>
</tr>
<tr>
<td>Degludec</td>
<td>30-90 min</td>
<td>12 hr</td>
<td>25 hr</td>
<td>42 hr</td>
</tr>
</tbody>
</table>

Insulin degludec injection (Tresiba®)

- **Contraindications**
  - Hypersensitivity
- **Caution in geriatric population**
  - May be less likely to recognize hypoglycemia
  - Use conservative dosing
- **Cost**
  - 100 unit/mL: ~$533/package
  - 200 unit/mL: ~$639/package

- **Adverse effects**
  - ≥5%
    - Hypoglycemia
    - Nasopharyngitis
    - Upper respiratory tract infection
    - Headache
    - Sinusitis
    - Gastroenteritis
  - Others
    - Weight gain
    - Peripheral edema
    - Hypokalemia
    - Lipodystrophy
    - Injection site reactions
Parathyroid hormone (Natpara®)

- **Indication**
  - Adjunct to calcium and vitamin D to control hypocalcemia in patients with hypoparathyroidism
  - ONLY for patients who cannot be well-controlled on calcium supplements and active forms of vitamin D alone
    - Potential risk osteosarcoma
- **REMS Program**
  - Restricted
  - Only certified healthcare professionals can prescribe
  - Only certified pharmacies can dispense
  - www.NATPARAREMS.com

- **Dosage and administration**
  - Individualized to achieve serum calcium level in the lower half of normal range
  - Confirm vitamin D stores sufficient and serum calcium >7.5 mg/dL
  - **Starting dose**
    - 50 mcg injected once daily in thigh
    - Can be increased every 4 weeks in increments of 25 mcg to max daily dose of 100 mcg if serum calcium cannot be maintained >8 mg/dL without active vitamin D/calcium
  - Decrease dose of vitamin D by 50% if calcium >7.5 mg/dL
  - Available as 25 mcg, 50 mcg, 75 mcg, 100 mcg
Parathyroid hormone (Natpara®)

- **Adverse effects (>10%)**
  - Parasthesia
  - Hypocalcemia
  - Headache
  - Hypercalcemia
  - Nausea
  - Hypoaesthesia
  - Diarrhea
  - Vomiting
  - Arthralgia
  - Hypercalciuria
  - Pain in extremity

- **Contraindications**
  - Patients at increased risk for osteosarcoma

- **Warnings & precautions**
  - Risk of osteosarcoma
  - Severe hypercalcemia/hypocalcemia
  - Digoxin toxicity

- **Monitoring**
  - Serum calcium levels every 3-7 days after starting/adjusting dose and when adjusting active vitamin D/calcium supplements

- **Cost:** $9975/vial
Miscellaneous
Pimavanserin (Nuplazid™)

• Indication
  ▫ Treatment of hallucinations and delusions associated with Parkinson’s disease psychosis

• MOA
  ▫ Atypical antipsychotic
  ▫ Potential effects mediated through a combination of inverse agonist and antagonist activity at serotonin 5-HT2A receptors and serotonin 5-HT2C receptors

• Dosage and administration
  ▫ 34 mg daily
    • Taken as two 17 mg tablets once daily without titration
Pimavanserin (Nuplazid™)

- **Adverse effects (≥5%)**
  - Peripheral edema
  - Confusional state
  - Leading to discontinuation
    - Hallucination, UTI, fatigue
- **Drug interactions**
  - Strong CYP3A4 inhibitors: reduce dose ½
  - Strong CYP3A4 inducers: monitor efficacy
    - Increased dose may be needed
- **Contraindications**
  - Not recommended in patients with hepatic impairment
- **Warnings & precautions**
  - Increased mortality in elderly patients with dementia-related psychosis
    - not approved for the treatment of patients with dementia-related psychosis unrelated to the hallucinations and delusions associated with Parkinson’s disease psychosis
  - QT interval prolongation
    - Avoid use with other drugs that increase QT interval
- **Cost:** $1950/60 tablets

Nuplazid (pimavanserin) [package insert].
**Selexipag (Uptravi®)**

- **Indication**
  - Treatment of pulmonary arterial hypertension (PAH, WHO Group I) to delay disease progression and reduce the risk of hospitalization for PAH

- **MOA**
  - Prostacyclin receptor agonist (IP receptor)
  - Hydrolyzed to active metabolite
    - 37-fold as potent as selexipag

- **Dosage and administration**
  - Starting dose: 200 mcg BID
  - Increase dose by 200 mcg BID at weekly intervals to highest tolerated dose
  - Max dose 1600 mcg BID
    - Maintenance dose determined by tolerability
  - Moderate hepatic impairment (Child-Pugh B)
    - Starting dose 200 mcg once daily
    - Increase the dose by 200 mcg once daily at weekly intervals
    - If dose missed ≥3 days, restart lower dose and titrate up
Selexipag (Uptravi®)

- **Adverse effects (≥5%)**
  - Headache
  - Jaw pain
  - Nausea
  - Vomiting
  - Myalgia
  - Pain in extremity
  - Flushing

- **Lab abnormalities**
  - Decrease in Hb, TSH

- **Drug interactions**
  - Avoid use with strong CYP2C8 inhibitors

- **Contraindications**
  - Do not use in severe hepatic impairment (Child-Pugh C)
  - Discontinue if pulmonary edema in patients with pulmonary veno-occlusive disease

- **Cost**
  - Ranges $11208-$26136
Lesinurad (Zurampic®)

• Indication
  ▫ Used in combination with xanthine oxidase inhibitor for treatment of hyperuricemia
    ▪ If target serum uric acid levels not achieved with xanthine oxidase inhibitor alone
  ▫ Not recommended for asymptomatic hyperuricemia
  ▫ Should NOT be used as monotherapy

• MOA
  ▫ Inhibits function of renal apical transporters that facilitate reabsorption of uric acid
    ▪ URAT1, OAT4
Lesinurad (Zurampic®)

• Dosage and administration
  ▫ 200 mg once daily
  ▫ Take with food and water

• Adverse effects (≥2%)
  ▫ Headache
  ▫ Influenza
  ▫ Increased SCr
  ▫ GERD
  ▫ Others
    ▫ Renal events
      ▫ Kidney stones, renal-related ADRs
    ▫ Major adverse CV events
      ▫ Causal relationship not established

• Monitoring
  ▫ Renal function
    ▪ Baseline
    ▪ Periodically as clinically indicated
  ▫ Contraindications
    ▫ Uric acid levels every 2-5 weeks, then every 6 months

• Contraindications
  ▫ Severe renal impairment (CrCL<30 ml/min), ESRD, kidney transplant, dialysis
    ▪ Do not initiate if CrCL<45 ml/min
  ▫ Severe hepatic impairment
  ▫ Tumor lysis syndrome or Lesch-Nyhan syndrome

Zurampic (lesinurad) [package insert].
Audience Assessment Question 4

Which of the following medications can cause a confusional state in patients?

a. Parathyroid hormone (Natpara®)
b. Pimavanserin (Nuplazid™)
c. Selexipag (Uptravi®)
d. Lesinurad (Zurampic®)
Patiromer for oral suspension (Veltassa®)

• Indication
  ▫ Treatment of hyperkalemia
  ▫ Should NOT be used as emergency treatment for life-threatening hyperkalemia
    • Delayed onset of action
• MOA
  ▫ Increases fecal potassium excretion by binding potassium in lumen of GI tract
    • Reduces free potassium in GI tract
    • Reduces serum potassium

• Dosage and administration
  ▫ 8.4 grams once daily with food
  ▫ Adjust dose by 8.4 grams daily as needed at one week intervals to obtain desired serum potassium
  ▫ Max dose 25.2 grams once daily
Patiromer for oral suspension (Veltassa®)

- **Adverse effects (≥2%)**
  - Constipation
  - Hypomagnesemia
  - Diarrhea
  - Nausea
  - Abdominal discomfort
  - Flatulence
- **Monitoring**
  - Potassium
  - Magnesium
- **Drug interactions**
  - Take other oral drugs 6 hours before or after
- **Contraindications**
  - Hypersensitivity
- **Warnings & precautions**
  - Worsening of GI motility
  - Hypomagnesemia
- **Cost**
  - Package size 4 packets: $142
  - Package size 30 packets: $714
Audience Assessment Question 5

Which of the following is the most appropriate situation in which to use patiromer for oral suspension (Veltassa®)?

a. Treatment of a potassium level of 6.2 mmol/L in a symptomatic patient
b. Treatment of a potassium level of 5.8 mmol/L in a patient on valsartan with diabetic gastroparesis
c. Treatment of a potassium level of 5.5 mmol/L in a patient on lisinopril with a past medical history of hypertension and myocardial infarction
Eluxadoline (Viberzi®)

- **Indication**
  - Treatment of irritable bowel syndrome with diarrhea (IBS-D)
- **C-IV**
- **MOA**
  - **Agonist**
    - Mu-opioid receptor
    - Kappa-opioid receptor
  - **Antagonist**
    - Delta-opioid receptor

- **Dosage and administration**
  - 100 mg BID with food
  - 75 mg BID with food in patients who:
    - Do not have a gallbladder
    - Unable to tolerate 100 mg dose
    - Receiving concomitant OATP1B1 inhibitors
    - Mild-moderate hepatic impairment
  - Discontinue in patients who develop severe constipation for >4 days
Eluxadoline (Viberzi®)

• Adverse effects (>5%)
  ▫ Constipation
  ▫ Nausea
  ▫ Abdominal pain
• Warnings & precautions
  ▫ Sphincter of Oddi spasm
  ▫ Pancreatitis
• Cost
  ▫ $1152/60 tablets

• Contraindications
  ▫ Known/suspected biliary duct obstruction
  ▫ Sphincter of Oddi disease/dysfunction
  ▫ Alcoholism/abuse/addiction
  ▫ Drink >3 alcoholic beverages/day
  ▫ History of pancreatitis
  ▫ Structural disease of pancreas
  ▫ Severe hepatic impairment (Child-Pugh C)
  ▫ Severe constipation or sequelae from constipation
  ▫ Suspected mechanical GI obstruction
## New Dosage Forms

<table>
<thead>
<tr>
<th>Generic</th>
<th>Brand</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Buprenorphine</td>
<td>Belbuca</td>
<td>New buccal film formulation for chronic pain management.</td>
</tr>
<tr>
<td>Morphine</td>
<td>Morphabond</td>
<td>An extended-release tablet formulation for severe chronic pain.</td>
</tr>
<tr>
<td>Oxycodone</td>
<td>Xtampza ER</td>
<td>New opioid formulation for chronic, severe pain.</td>
</tr>
<tr>
<td>Naloxone</td>
<td>Narcan</td>
<td>New nasal spray formulation for emergency treatment of opioid overdose.</td>
</tr>
<tr>
<td>Tofacitinib</td>
<td>Xeljanz XR</td>
<td>New extended-release tablet formulation for rheumatoid arthritis.</td>
</tr>
<tr>
<td>Carbidopa/levodopa</td>
<td>Duopa</td>
<td>New enteral suspension formulation for patients with advanced Parkinson’s disease.</td>
</tr>
<tr>
<td>Carbidopa/levodopa</td>
<td>Rytary</td>
<td>New extended-release capsule formulation for Parkinson’s disease and other forms of parkinsonism.</td>
</tr>
<tr>
<td>Aspirin</td>
<td>Durlaza</td>
<td>Extended-release formulation for secondary prevention CV events.</td>
</tr>
<tr>
<td>Lamivudine/raltegravir</td>
<td>Dutrebis</td>
<td>Combination product for treatment of HIV-1 infection.</td>
</tr>
<tr>
<td>Atazanvir/cobicistat</td>
<td>Evotaz</td>
<td>A protease inhibitor and pharmacokinetic booster for HIV-1 infection.</td>
</tr>
<tr>
<td>Darunavir/cobicistat</td>
<td>Prezcobix</td>
<td>A protease inhibitor and pharmacokinetic booster for HIV-1 infection.</td>
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## New Dosage Forms

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<tr>
<td>Emtricitabine/tenofovir alafenamide</td>
<td>Descovy</td>
<td>New combination oral tablet for HIV-1 infection.</td>
</tr>
<tr>
<td>Emtricitabine/rilpivirine/tenofovir alafenamide</td>
<td>Odefsey</td>
<td>New combination oral tablet for HIV-1 infection.</td>
</tr>
<tr>
<td>Empagliflozin/linagliptin</td>
<td>Glyxambi</td>
<td>New combination SGLT2 inhibitor and DPP-4 inhibitor for type 2 diabetes.</td>
</tr>
<tr>
<td>Empagliflozin/metformin</td>
<td>Synjardy</td>
<td>New combination SGLT2 inhibitor and metformin for type 2 diabetes.</td>
</tr>
<tr>
<td>Insulin degludec/insulin aspart</td>
<td>Ryzodeg</td>
<td>A 70/30 mix insulin analog for diabetes.</td>
</tr>
<tr>
<td>Insulin glargine</td>
<td>Toujeo</td>
<td>New U-300 strength long-acting insulin for diabetes.</td>
</tr>
<tr>
<td>Paliperidone</td>
<td>Invega Trinza</td>
<td>New longer-acting (e.g., 3 month) injectable atypical antipsychotic.</td>
</tr>
<tr>
<td>Perindopril/amldipine</td>
<td>Prestalia</td>
<td>New combination ACEI and calcium channel blocker for hypertension.</td>
</tr>
<tr>
<td>Glycopyrrolate</td>
<td>Seebri Neohaler</td>
<td>New anticholinergic oral inhaler for COPD.</td>
</tr>
<tr>
<td>Glycopyrrolate/formoterol</td>
<td>Bevespi Aerosphere</td>
<td>New combination anticholinergic/LABA for COPD.</td>
</tr>
<tr>
<td>Tiotropium/olodaterol</td>
<td>Stiolti Respimat</td>
<td>New combination long-acting anticholinergic/beta-agonist oral inhaler for COPD.</td>
</tr>
</tbody>
</table>
Conclusions

• Significant number of medications approved over past 18 months

• Majority of medications have limited number of geriatric patients included in studies
  ▫ Consider increased sensitivity in geriatric population
  ▫ Monitor closely for adverse events
References

7. Praxbind (idarucizumab) [prescribing information]. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals, Inc; 2015.
References