New Drugs: How Do They Stack Up?

Advanced Pharmacology Update
University of Southern Indiana

September 26, 2014
Trish Rippetoe Freeman, RPh, PhD
Associate Professor, Pharmacy Practice and Science
University of Kentucky College of Pharmacy

Learning Objectives

At the conclusion of this program, the participant should be able to:
- Identify select new molecular and biological entities, with the exception of diagnostic compounds, that entered the US market in 13-14
- Describe each agent's clinical use, mechanism of action, dosage, adverse reactions, contraindications, and drug interaction profile
- Compare new medicines with other agents used for the same indications

Learning Objectives

At the conclusion of this program, the participant should be able to:
- List special patient instruction and monitoring parameters for each of these agents
- Review new guidelines for chronic diseases such as hypertension, diabetes and hypercholesterolemia
- Identify recent FDA safety issues with select drugs
Learning Objectives

• Review use of KASPER system
• Discuss recent trends in KASPER use and CS prescribing since the enactment of HB1
• Identify changes in CS law affecting prescribers
• Discuss new pain medications, pain management principles and naloxone co-prescribing to promote safe prescribing of opioids

Categories of NDAs

• New molecular entities (NMEs)
  - New drug products that contain a chemical substance as their active ingredient, marketed for the first time in the US
• New biologics
  - Vaccines or blood products
• New indications
• New dosage forms
• New generic forms

New Cardiovascular Drugs
Riociguat (Adempas)

- Soluble guanylate cyclase stimulator
- Indicated to improve functional class and exercise capacity and delay clinical progression in patients with
  - persistent chronic thromboembolic pulmonary hypertension
  - pulmonary arterial hypertension

Riociguat (Adempas)

- Mechanism of Action:

Riociguat (Adempas)

- Recommended dose
  - 1 mg TID
  - May start at 0.5mg TID in patients at risk for hypotension
  - Increase by 0.5mg increments at 2-week intervals to maximum of 2.5 mg TID
    - Higher doses may be required in patients who smoke

- Contraindications
  - Concurrent use of nitrates/nitric oxide donors
  - Pregnancy (Category X)
  - Concurrent use of PDE inhibitors
Drugs in Pregnancy

**Riociguat (Adempas)**

- **Warnings/Precautions**
  - Hypotension
  - Bleeding (pulmonary)
  - Pulmonary edema
  - Not recommended for use in patients with CrCL <15 mL/min or on dialysis

- **Drug interactions**
  - Strong CYP and P-gp inhibitors
    - Start at 0.5 mg and monitor for hypotension
  - Antacids
    - Separate administration by 1 hour
Contraindication vs. Warning

- **Contraindication**
  - Relative
  - Absolute

- **Warning/Precaution**
  - Think carefully about use in specific populations/circumstances
  - Risk vs. benefit

Riociguat (Adempas)

- **Adverse effects**
  - Headache
  - Dizziness
  - Low BP
  - Peripheral edema
  - N/V/D

Vorapaxar (Zontivity)

- New class of antiplatelet to reduce thrombotic CV events in patients with history of MI or peripheral arterial disease
  - Protease-activated receptor-1 (PAR-1) antagonist
  - Reduces rate of CV death, MI, stroke, urgent coronary revascularization
Vorapaxar (Zontivity)

- **Mechanism of Action**
  - Reversible antagonist of the PAR-1 receptor expressed on platelets
  - Effectively irreversible due to long t1/2
  - Significant inhibition of platelet function up to 4 weeks following d/c
  - Inhibits thrombin-induced and thrombin receptor agonist peptide (TRAP)-induced platelet aggregation
  - Does NOT appear to inhibit ADP, collagen or thromboxane induced platelet aggregation

Vorapaxar (Zontivity)

- **Recommended dose**
  - 2.08 mg tablet (equivalent to 2.5 mg Vorapaxar sulfate) daily
  - Use with aspirin and/or clopidogrel per standard of care

- **Contraindications**
  - History of stroke, TIA or ICH
  - Active pathological bleeding
Vorapaxar (Zontivity)

- Adverse Effects
  - Depression
  - Anemia
  - Rash

- Warnings
  - Bleeding, including ICH and fatal bleeding
    - Older age, low body weight, reduced renal/hepatic function are risk factors
    - Use of anticoagulants, NSAIDs, SSRIs and SNRIs increase bleeding risk
    - No reversal agent

- Avoid concurrent use of strong CYP3A inhibitors or inducers

Review of CYP Enzymes
PO Drug Bioavailability

CYP3A4

• Drugs can be
  - Substrates
  - Inhibitors
    - A Strong inhibitor is one that causes a >5-fold increase in the plasma AUC values or more than 80% decrease in clearance
    - A Moderate inhibitor is one that causes a >2-fold increase in the plasma AUC values or 50-80% decrease in clearance
    - A Weak inhibitor is one that causes a >1.25-fold but <2-fold increase in the plasma AUC values of 20-50% decrease in clearance
    - All other inhibitors
  - Inducers

http://medicine.iupui.edu/clinpharm/ddis/main-table/
JNC 8: Guidelines for Treatment of High Blood Pressure

Dosing Strategies
Figure 1: Illustrating risk factors in individuals with chronic kidney disease (CKD) (A) and pathways of intervention (B) (adapted from [1, 2, 3, 4]).

(A) Risk factors for CKD progression:
- Hypertension
- Diabetes mellitus
- Obesity
- Family history of kidney disease
- Advanced age
- Smoking
- Chronic infections
- Medications (e.g., diuretics, nonsteroidal anti-inflammatory drugs)
- Alcohol consumption
- Malnutrition

(B) Pathways of intervention:
1. Diet and fluid management
2. Exercise
3. Medication adjustment
4. Dialysis
5. Transplantation
6. Surgical procedures

Figure 2: Algorithm for initiating statin therapy in individuals with chronic kidney disease (adapted from [5]).

1. Measure eGFR and lipid levels.
2. If eGFR < 60 mL/min/1.73 m², measure albuminuria.
3. If albuminuria is high, consider ACE inhibitors/ARBs.
4. If eGFR < 30 mL/min/1.73 m², consider hemodialysis.
5. If eGFR < 15 mL/min/1.73 m², consider peritoneal dialysis.
6. If statin intolerance, consider alternative lipid-lowering therapies.

Figure 3: Schematic diagram of the management of chronic kidney disease (adapted from [6]).

1. Identification of CKD risk factors.
2. Initiation of preventive interventions.
4. Adjustments to medication regimens.
5. Referral to nephrologist for advanced care.

Figure 4: Flowchart for the management of chronic kidney disease (adapted from [7]).

1. Assess renal function and comorbid conditions.
2. Initiate antihypertensive therapy.
3. Consider statin therapy based on risk profile.
4. Monitor progress and adjust treatment accordingly.
5. Refer to nephrologist for specialized care.

Figure 5: Algorithm for the management of chronic kidney disease (adapted from [8]).

1. Assess renal function and comorbidity status.
2. Initiate appropriate medications.
3. Monitor progress and adjust therapy as needed.
4. Refer to nephrologist for advanced care.
5. Educate patient on lifestyle modifications.

References:
New Endocrine Drugs

Albiglutide (Tanzeum)
- GLP-1 receptor agonist (fusion protein) indicated as an adjunct to diet and exercise to improve glycemic control in adults with T2DM
  - Joins exenatide (Byetta, Bydureon) and liraglutide (Victoza)
- Studied alone and in combination with metformin, glimepiride, pioglitazone, and insulin
- Not indicated for T1DM or as first line monotherapy in T2DM

Albiglutide (Tanzeum)
- Mechanism of Action
  - Incretin analogue
  - Lowers blood glucose and A1c by activating GLP-1 (incretin) receptors in GI tract
    - GLP 1 increases insulin secretion from pancreas
    - Delays gastric emptying time
    - Decreases glucagon production in liver
Albiglutide (Tanzeum)

- Dosage and administration
  - 30 mg subcutaneously once weekly
  - Increased to 50 mg once weekly in patients requiring additional glycemic control
  - Administer at any time of day, without regard to meals
  - Inject subcutaneously in the abdomen, thigh, or upper arm
  - If a dose is missed, administer within 3 days
Albiglutide (Tanzeum)

• Warnings
  - Pancreatitis
  - Thyroid C-cell tumors in animals
    • FDA required pharmacovigilance study
  - Hypoglycemia
  - Gastroparesis
  - Renal impairment (avoid in severe or end stage)

Albiglutide (Tanzeum)

• Adverse effects
  - GI (nausea/vomiting, diarrhea/constipation, bloating)
  - Headache
  - Injection site reactions
  - Hypersensitivity reactions
  - Hypoglycemia if given with sulfonylurea

Dulaglutide (Trulicity)

• Another GLP-1 receptor agonist indicted as an adjunct to diet and exercise to improve glycemic control in adults with T2DM
• Studied alone and in combination
• Not indicated for T1DM or as first line monotherapy in T2DM
• Administered weekly by subcutaneous injection
• Similar AEs, warnings and precautions as Tanzeum
Empagliflozin (Jardiance)

- Sodium-glucose co-transporter 2 (SGLT2) inhibitor indicated as adjunct to diet and exercise to improve glycemic control in T2DM
- Mechanism of action:

Empagliflozin (Jardiance)

- **Recommended dose:**
  - 10 mg once daily in the AM, with or without food
  - May increase as needed to 25 mg once daily
  - Do not use if eGFR falls below 45 ml/min/1.73 m²
  - D/C if eGFR falls persistently below 45

Empagliflozin (Jardiance)

- **Adverse effects**
  - UTI
  - Yeast infection in women
Empagliflozin (Jardiance)

- **Contraindications**
  - History of hypersensitivity to empagliflozin
  - Severe renal impairment, ESRD, dialysis

- **Warnings/precautions**
  - Hypotension
  - Impairment in renal function
  - Hypoglycemia
  - Genital mycotic infections and urinary tract infections
  - Increased LDL-C

Canagliflozin and metformin (Invokamet)

- New combination of SGLT2 inhibitor and biguanide indicated as adjunct to diet and exercise to improve glycemic control in adults with T2DM not adequately controlled on either medication as monotherapy

Human Insulin Inhalation Powder (Afrezza)

- Rapid acting inhaled insulin to improve glycemic control in adult patients with diabetes
  - In T1DM, must be used in combination with long-acting insulin

- **Dosage and administration:**
  - Available in single use cartridges of 4 and 8 units
  - Dosage individualized
  - Administer dose at beginning of meal
**Human Insulin Inhalation Powder (Afrezza)**

Figure 1. Measured AFREZZA Dose Conversion Table

<table>
<thead>
<tr>
<th>Inhaled Mediation Range (U)</th>
<th>AFREZZA Dose</th>
<th>Oral Dose (mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>up to 4 units</td>
<td>4 units</td>
<td>12 IU</td>
</tr>
<tr>
<td>5-8 units</td>
<td>8 units</td>
<td>16 IU</td>
</tr>
<tr>
<td>9-12 units</td>
<td>12 units</td>
<td>20 IU</td>
</tr>
<tr>
<td>13-16 units</td>
<td>16 units</td>
<td>24 IU</td>
</tr>
<tr>
<td>17-20 units</td>
<td>20 units</td>
<td>30 IU</td>
</tr>
<tr>
<td>21-24 units</td>
<td>24 units</td>
<td>36 IU</td>
</tr>
</tbody>
</table>


**Contraindications**
- Chronic lung disease including COPD and asthma
  - assess for lung disease via history, physical exam and FEV1 before initiating use, at 6 months and then annually thereafter

**Warnings/precautions**
- Avoid in smokers
- May cause acute bronchospasm
- Hypoglycemia
- DKA
- hypokalemia

**Adverse effects:**
- Hypoglycemia
- Cough
- Throat irritation
- Throat pain
New Diabetes Guidelines

Table 2—Criteria for the diagnosis of diabetes

- Fasting plasma glucose (FPG) ≥ 126 mg/dL (≥ 7.0 mmol/L) or
- 2-hour post-OGTT plasma glucose (2h-PG) ≥ 200 mg/dL (≥ 11.1 mmol/L) or
- Hemoglobin A1C (HbA1c) ≥ 6.5% ≥ 48 mmol/mol)

In a patient with classical symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose ≥ 200 mg/dL (≥ 11.1 mmol/L)

Table 6—Summary of glycemic recommendations for many nonpregnant adults with diabetes

- Preprandial capillary plasma glucose < 130 mg/dL (≤ 7.2 mmol/L)
- 2h-PG < 180 mg/dL (≤ 10.0 mmol/L)

Note: These recommendations are based on the American Diabetes Association's evidence-based guidelines. They are intended to guide management decisions and should be tailored to individual patient needs and preferences. The specific targets may vary depending on factors such as age, comorbidities, and patient preference. These guidelines are subject to change as new evidence becomes available.
Testosterone gel (Natesto)

- Intranasal form of testosterone for primary hypogonadism and hypogonadotropic hypogonadism
- 11 mg (2 actuations; one per nostril) three times daily
- Serum total testosterone concentrations should be checked after one month
- D/C when the total testosterone concentration consistently exceeds 1050 ng/dL
New Respiratory Medications

Umeclidinium (Incruse Ellipta)
• Long-acting anticholinergic (ACH) or long-acting muscarinic antagonist (LAMA)
• Indicated for maintenance treatment of chronic obstructive pulmonary disease (COPD), including chronic bronchitis and/or emphysema
• One inhalation once daily (62.5 mcg)

Umeclidinium and Vilanterol (Anoro Ellipta)
• First once-daily combination anticholinergic (LAMA) and LABA inhaler
• Indicated for once-daily maintenance treatment of COPD
• Recommended dose
  – One inhalation (62.5/25 mcg) once daily
• Adverse effects/warnings
  – Same as with other LABA/ACH inhalers
Fluticasone furoate (Arnuity Ellipta)

- Once daily inhaled corticosteroid for treatment of asthma as prophylactic therapy in patients aged 12 years and older
- Available in 100 and 200 mcg strengths
- Recommended dose:
  - 1 inhalation daily based on severity of disease
- Contraindicated in patients with severe milk allergy
- Not for relief of acute bronchospasm

Olodaterol (Striverdi Respimat)

- New LABA for patients with COPD/emphysema
- Two inhalations once daily
- Not for use in acute COPD exacerbations
- Not for use in asthma
- Same AEs as other LABAs

New COPD Guidelines

Dalbavancin (Dalvance)

- **New injectable anti-infective for treatment of acute bacterial skin and skin structure infections (ABSSSI)**
- **Active against gram-positive organisms, including**
  - MSSA, MRSA
  - Strep pyogenes, agalactiae and anginosus

**Dalbavancin (Dalvance)**

**Mechanism of Action**
- A lipoglycopeptide that interferes with cell wall synthesis
- Bacteriocidal
- Synergistic with oxacillin

**Recommended dose**
- Two dose regimen
  - 1000mg dose infused over 30 min followed by 500mg one week later
  - 750 mg followed by 375 mg one week later in patients with CrCl <30 ml/min
Creatinine Clearance

• Studies estimate for high renal clearance drugs, 25-50% of patients may be receiving inappropriate doses
• All drug dosing recommendations made using Cockcroft-Gault equation

\[
CrCl = \frac{(140 - \text{age}) \times \text{weight (kg)}}{\text{Scr} \times 72} \times 0.85 \text{ for females}
\]

http://nephron.com/cgi-bin/CGSI.cgi

Dalbavancin (Dalvance)

• Warnings
  - Hypersensitivity reactions
  - Infusion reactions
  - ALT elevations
  - C Diff infections
• Adverse effects
  - Nausea, diarrhea
  - Headache

Oritavancin (Orbactiv)

• New lipoglycopeptide antibacterial drug indicated for acute bacterial skin and skin structure infections caused by susceptible isolates of designated gram positive organisms
  - MSSA, MRSA
  - Strep pyogenes, agalactia, dysalactia, anginosus
  - VSE
• Not for use in patients with confirmed or suspected osteomyelitis
Oritavancin (Orbactiv)

• Mechanism of Action
  - Cell wall synthesis inhibitor

• Recommended dose:
  - Single 1200 mg dose administered by IV infusion over 3 hours

• Contraindications
  - Known hypersensitivity
  - Use of IV UFH within 48 hours after dose

Oritavancin (Orbactiv)

• Warnings/precautions
  - Warfarin – increased exposure and risk for bleeding
  - Coagulation test interference – prolongs aPPT for up to 48 hrs and PT and INR for up to 24 hours
  - Hypersensitivity reactions
  - Infusion reactions
  - C diff

• Adverse effects
  - Headache, N/V, diarrhea

Tedizolid (Sivextro)

• New oxazolidinone-class antibacterial drug indicated in adults for the treatment of acute bacterial skin and skin structure infections (ABSSSI) caused by designated susceptible bacteria
  - MSSA, MSRA
  - Strep species
  - Enterococcus faecalis

• Joins linezolid (Zyvox)
Tedizolid (Sivextro)

- Recommended dose:
  - 200mg IV or PO once daily x 6 days
- Warnings
  - C diff
  - Not evaluated in patients with neutropenia, consider alternate therapies
- Adverse effects
  - N/V
  - Diarrhea
  - Headache
  - Dizziness

Posaconazole (Noxafil)

- Azole antifungal indicated for prophylaxis of invasive Aspergillus and Candida infections in immunocompromised patients
  - Originally approved (2006) as oral suspension for oropharyngeal candidiasis treatment
  - New dosage forms include tablets (100mg) and injection 18 mg/mL

Posaconazole (Noxafil)

- Recommended dose (IV and PO Tabs)
  - 300 mg BID on 1st day, then 300 mg daily
  - Duration of therapy based on recovery from neutropenia/immunosuppression
- Contraindications
  - Hypersensitivity to azole antifungals
  - Concurrent therapy with:
    - Sirolimus
    - CYP3A4 substrates pimozide and quinidine (QTc prolongation and TdP)
    - HMG-CoA reductase inhibitors that are CYP3A4 substrates (rhabdo)
Posaconazole (Noxafil)

- Warnings/Precautions
  - QTc prolongation and TdP
  - Hepatotoxicity
  - Moderate to severe renal impairment (CrCl <50 mL/min) - injection only
- Adverse effects
  - Diarrhea
  - Nausea/vomiting
  - Headache
  - Hypokalemia

Luliconazole (Luzu)

- Azole antifungal cream indicated for the topical treatment of interdigital tinea pedis, tinea cruris, and tinea corporis in patients 18 years of age and older
- Apply to affected area once daily x 1-2 weeks depending on indication
- May cause application site reactions
- 1% cream available

Tavaborole (Kerydin)

- An oxaborole antifungal indicated for the topical treatment of onychomycosis of the toenails
- Apply to affected toenails once daily for 48 weeks
- 5% topical solution
- May cause application site reactions
  - Redness
  - Exfoliation
  - Dermatitis
Efinaconazole (Jublia)
• Another new azole antifungal for treatment of onychomycosis of the toenails
• Apply to affected toenails once daily x 48 weeks using “flow-through brush applicator”
• 10% topical solution
• Application site reactions are only significant AEs

Other New Dosage Forms
• Econazole (Ecoza)
  - Azole antifungal foam for treatment of interdigital tinea pedis in patients age 12 and older
  - Apply once daily for 4 weeks
  - Avoid heat, flame and/or smoking during and immediately following application

New Nervous System Medications
Tasimelteon (Hetlioz)

- Melatonin receptor agonist for treatment of non-24-hour sleep-wake disorder
  - Sleep condition caused by inability to regulate body clock by recognizing light from dark in blind individuals
- Agonist at both MT1 and MT2 receptors involved in control of circadian rhythms
  - Same as ramelteon (Rozerem)
- Recommended dose
  - 20 mg prior to bedtime
  - Take on empty stomach, without food

Tasimelteon (Hetlioz)

- Precautions
  - Improvement in sleep wake cycle may not be immediate
- Adverse effects
  - Headache
  - Nightmares, unusual dreams
  - Elevated liver enzymes
- Drug interactions
  - CYP1A2 inhibitors
  - CYP3A4 inducers

Eslicarbazepine (Aptiom)

- New antiepileptic medication indicated for treatment of partial onset seizures
  - Similar to oxcarbazepine
- Mechanism of action
  - Unknown, thought to involve inhibition of voltage-gated sodium channels
- Recommended dose
  - 400 mg once daily x 1 week, then increase to 800 mg daily (recommended dose)
  - Maximum dose 1200 mg daily
  - Reduce dose in renal insufficiency
Eslicarbazepine (Aptiom)

- **Adverse Effects**
  - Dizziness
  - Somnolence
  - Nausea/vomiting
  - Headache, diplopia
  - Vertigo, tremor, ataxia

- **Warnings/precautions**
  - Dermatologic reactions
  - Drug reaction with eosinophilia
  - Angioedema and anaphylaxis

---

Figure 2: Potential Impact of AEDs on the AUC of Non-AEDs

<table>
<thead>
<tr>
<th>Change in</th>
<th>Point Change and 95% CI</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>0.0</td>
<td>None</td>
</tr>
<tr>
<td>Increase</td>
<td>1.0</td>
<td>None</td>
</tr>
<tr>
<td>Decrease</td>
<td>0.0</td>
<td>None</td>
</tr>
</tbody>
</table>

- Dosage should be reduced to maintain AUC

---

Figure 3: Impact of Interactions on AUC of Eslicarbazepine

<table>
<thead>
<tr>
<th>Change due to</th>
<th>Point Change and 95% CI</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>0.0</td>
<td>None</td>
</tr>
<tr>
<td>Increase</td>
<td>1.0</td>
<td>None</td>
</tr>
<tr>
<td>Decrease</td>
<td>0.0</td>
<td>None</td>
</tr>
</tbody>
</table>

- Dosage should be adjusted to maintain AUC

---
Suvorexant (Belsomra)

- New class of sedative/hypnotics classified as an orexin (hypocretin) receptor antagonist
  - Orexin neuropeptide signaling system in a central promoter of wakefulness
    - Narcolepsy/cataplexy caused by a deficiency in orexin
    - Blocking the binding of wake-promoting neuropeptides orexin A and orexin B to the OX1R and OX2R suppresses the wake drive

Central Effects of Orexins

Suvorexant (Belsomra)

- Indication:
  - treatment of insomnia, characterized by difficulties with sleep onset and/or maintenance
- Recommended dose:
  - 10 mg no more than once per night taken within 30 min of going to bed, with at least 7 hours remaining before planned time of awakening
  - Maximum dose 20 mg once nightly
  - Take on empty stomach to avoid delayed onset of effect
Suvorexant (Belsomra)

- **Contraindications:**
  - Narcolepsy

- **Warnings/precautions (dose dependent):**
  - Daytime somnolence
  - Impaired driving and motor coordination
  - Depression or suicidal thinking
  - Compromised respiratory function
  - Sleep paralysis, hypnagogic and hypnopompic hallucinations, cataplexy-like symptoms

- **Adverse Effects**
  - Daytime somnolence

- **Drug interactions:**
  - CYP3A Inhibitors
    - Use 5mg dose when used with moderate CYP3A inhibitors
    - Avoid in patients on strong CYP3A inhibitors
  - Digoxin
    - Monitor levels

- Available in 5, 10, 15 and 20 mg tablets

New Dosage Forms

- **Desvenlafaxine (Khedezla)**
  - Extended release form of desvenlafaxine
    - Similar to Pristiq
  - SNRI for major depressive disorder
  - 50 mg daily, up to 400 mg max dose
  - Osmotic dosage form (matrix shell will pass in stool)
Other New Dosage Forms

- **Topiramate (Qudexy XR)**
  - Extended release form of topiramate
  - Indicated for partial onset and generalized tonic-clonic seizures and Lennox-Gastaut Syndrome
  - Same adverse effects/warnings as with other topiramate products
    - Anorexia, weight loss
    - Fatigue, somnolence, difficulty with memory, concentration, attention, cognition

Topiramate (Qudexy XR)

New FDA Safety Warnings

- Lunesta and risk of next day impairment
- Heart failure risk with saxagliptin?
- Doribax and increased risk of death in patients with ventilator associated pneumonia
- Increased risk of GI bleed with Pradaxa compared to warfarin, but Pradaxa decreased risk of stroke compared

New FDA Safety Warnings


• Fluooroquinolones and peripheral neuropathy
• Ketoconazole and fatal liver toxicity, drug interactions = new limits on use and new med guide
• Ambien CR and risk of next morning impairment
• Valproic acid use during pregnancy and decreased IQ scores in exposed children

New FDA Safety Warnings


• Azithromycin and QTc prolongation
• Pancreatitis and pre-cancerous pancreas changes with incretin mimetics
• Codeine now contraindicated for use in children following tonsillectomy and adenoidectomy
• Pradaxa should not be used in patients with mechanical prosthetic valves

Medication Safety: What can you do?

• Only prescribe drugs when absolutely necessary
• Revisit continued need for medications at regular intervals
• Document creatinine clearance and adjust doses accordingly
• Consider CYP profile of drugs prescribed
• If medication needed to treat adverse effect of another medication, consider alternative therapy first
Resources for New Drugs and Guidelines

- National Guideline Clearinghouse
  http://www.guideline.gov/
- Drugs@fda.gov
  http://www.accessdata.fda.gov/Scripts/cder/drugsatfda/index.cfm
- Centerwatch
  http://www.centerwatch.com/

New Pain Medications, Pain Management, Opioid Overdose Prevention and KASPER

Hydrocodone ER (Zohydro)

- New extended release form of hydrocodone
- Indicated for pain severe enough to require daily, around the clock, long-term opioid treatment
- Risk of addiction, abuse and misuse has made marketing of Zohydro controversial
Hydrocodone ER (Zohydro)

- Recommended dose
  - 10 mg every 12 hours
  - May increase in 10 mg increments every 3 – 7 days as needed to achieve adequate analgesia
  - Swallow whole; do not crush, chew or dissolve
  - 10, 15, 20, 30, 40 and 50 mg capsules available
Oxycodone and APAP ER (Xartemis XR)

- Extended release combination of oxycodone and acetaminophen (7.5/325 mg)
- Indication
  - Acute pain severe enough to require opioid treatment and for which alternative treatment options are inadequate
- Recommended dose
  - 2 tablets every 12 hours
  - Do not break, crush, cut, dissolve, or split tablets

Oxycodone and Naloxone ER (Targiniq ER)

- Combination product consisting of oxycodone, an opioid agonist, and naloxone, an opioid antagonist
- Indicated for the management of pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate
**Oxycodone and Naloxone ER (Targiniq ER)**

- **Limitations of Use**
  - Because of the risks of addiction, abuse, and misuse with opioids, even at recommended doses, and because of the greater risks of overdose and death with extended-release formulations, reserve TARGINIQ ER for use in patients for whom alternative treatment options (e.g., non-opioid analgesics or immediate-release opioids) are ineffective, not tolerated, or would be otherwise inadequate to provide sufficient management of pain.

- **Limitations of Use**
  - TARGINIQ ER is not indicated as an as-needed (prn) analgesic.
  - Total daily dose should not exceed 80 mg/40 mg (40 mg/20 mg q12h) because higher doses may be associated with symptoms of opioid withdrawal from naloxone component.

- **Recommended dose:**
  - For opioid-naive and opioid non-tolerant patients, initiate with 10 mg/5 mg every 12 hours.
  - Tablets must be swallowed intact and are not to be cut, broken, chewed, crushed, or dissolved (risk of potentially fatal dose).
Oxycodone and Naloxone ER (Targiniq ER)

- Dose considerations:
  - Initiation of strong CYP3A4 inhibitor could precipitate opioid overdose from accumulation of oxycodone
  - Use ½ usual dose in patients with hepatic or renal impairment
  - Do not abruptly discontinue in a physically dependent patient
Buprenorphine and Naloxone buccal film (Bunavail)

• Partial opioid agonist/antagonist for maintenance treatment of opioid dependence
• Joins Subuxone and Zubsolv
• Naloxone in product blocks euphoria and may precipitate withdrawal if patients misuse product
• Must have X-license to prescribe

Pain Management Guidelines

Guidelines for use of opioids in chronic non-cancer pain

• From the American Pain Society
• Make recommendations for risk assessment, contracts, screening and monitoring
• Available at:
**Scoring Instructions for the SOMAI® Version 1.0-1.0**

To score the SOMAI®, only apply enteral staging of the disease

<table>
<thead>
<tr>
<th>Item</th>
<th>Factor</th>
<th>Explanation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>History of Substance Abuse</td>
<td>Alcohol, drugs, prescribed drugs</td>
</tr>
<tr>
<td>2.</td>
<td>Personality</td>
<td>Antisocial Behavior, Psychopathy, Borderline, Narcissistic, Impulsive</td>
</tr>
<tr>
<td>3.</td>
<td>Psychiatric History</td>
<td>Antisocial Behavior, Psychopathy, Borderline, Narcissistic, Impulsive</td>
</tr>
</tbody>
</table>

**Score Interpretation**

- **Low Risk**: Score 0-1
- **Moderate Risk**: Score 2-3
- **High Risk**: Score 4

**SOMAI Scoring Example**

<table>
<thead>
<tr>
<th>Item</th>
<th>Factor</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>History of Substance Abuse</td>
<td>1</td>
</tr>
<tr>
<td>2.</td>
<td>Personality</td>
<td>2</td>
</tr>
<tr>
<td>3.</td>
<td>Psychiatric History</td>
<td>1</td>
</tr>
</tbody>
</table>

Total Score: 4
Opioid Overdose Prevention with Naloxone
Naloxone Access Laws

- Kentucky joined several other states last session when enacted naloxone access law
- Allows prescribing of naloxone to a third party for administration to patients at risk for opioid (and heroin) overdose
- Most naloxone rescue administered intranasally using naloxone injection with atomizer
- One new FDA approved product for subq administration available

Naloxone HCl (Evzio)

- Auto-injector of naloxone for emergency treatment of known or suspected opioid overdose
  - Electronic voice instruction system
- 0.4 mg administered IM or SQ
  - Anterolateral aspect of the thigh
  - Can administer through clothing
  - Repeat q 2 -3 min prn until emergency medical assistance arrives

Naloxone HCl (Evzio)

- Warnings
  - Acute abstinence syndrome
    - Body aches
    - N/V/Diarrhea
    - Hypertension, tachycardia
    - Sweating
    - Shivering, trembling
    - Nervousness, restlessness, irritability
Patient Education

- Store at room temperature; use before expiration date
- How to use Evzio
- How to recognize signs and symptoms of opioid overdose
  - Extreme sleepiness
  - Respiratory depression
  - Pinpoint pupils
  - Bradycardia and hypotension

Note:
EVZIO makes a distinct sound (click and hiss) when it is pressed against the thigh. This is normal and means that EVZIO is working correctly. Keep EVZIO firmly pressed on the thigh for 5 seconds after you hear the click and hiss sound. The needle will inject and then retract back up into the EVZIO auto-injector and is not visible after use.

http://www.evzio.com/hcp
KASPER Update

What is KASPER?

- The Kentucky All Schedule Prescription Electronic Reporting System (KASPER) tracks controlled substance prescriptions dispensed within the state.
- A KASPER report shows all scheduled prescriptions for an individual over a specified time period, the prescriber and the dispenser.
- Enhanced KASPER (eKASPER) provides Web-based access to KASPER data.
- KASPER is a reporting system designed to be a source of information for practitioners and pharmacists and an investigative tool for law enforcement.

How to Use KASPER

- Web training video available on the KASPER website.
  - [http://training.chfs.ky.gov/KASPER_1/KASPER_1.swf](http://training.chfs.ky.gov/KASPER_1/KASPER_1.swf)
Important Changes Relative to KASPER Reports

• Effective July 20, 2012
  – Can be shared among treatment providers
  – Can be shared with patient being treated
  – Can be placed in the medical record
    • Becomes permanent part of record
    • Is discoverable

---

**Prescribing Checklist**

Before prescribing a controlled substance:

1. Gather patient’s medical history; conduct patient examination and document everything as the patient’s medical record. (Each provider will maintain a complete record.)
2. Query KASPER for all available data on the patient.
3. Make a written treatment plan that states the objectives of the treatment and any additional diagnosis required.
4. Include an advantage that includes a history of the use of controlled substances.
5. Discuss the risks and benefits of the use of controlled substances with the patient, including the risk of tolerance and drug dependence for drugs with the patient’s treatment, or with the patient’s legal provider on health care services.

For subsequent prescriptions:

7. Obtain necessary updates on the patient’s medical condition and modify the treatment plan as necessary.
8. Query the KASPER for at least once every three months during the course of treatment before renewing a new prescription or will lose the controlled substance.

---

**Scheduled Drug Laws for APRNs at a Glance**

<table>
<thead>
<tr>
<th>Schedule</th>
<th>APRN (nurse)</th>
<th>Prescriber</th>
<th>Allowed Efforts</th>
<th>Maximum Daily Dose</th>
<th>Maximum Total Dose</th>
<th>Required Documentation</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>APRN (nurse)</td>
<td>Prescriber</td>
<td>10 mg</td>
<td>10 mg</td>
<td>100 mg</td>
<td>Controlled substance reports</td>
</tr>
<tr>
<td>3</td>
<td>APRN (nurse)</td>
<td>Prescriber</td>
<td>20 mg</td>
<td>20 mg</td>
<td>200 mg</td>
<td>Controlled substance reports</td>
</tr>
<tr>
<td>7</td>
<td>APRN (nurse)</td>
<td>Prescriber</td>
<td>50 mg</td>
<td>50 mg</td>
<td>500 mg</td>
<td>Controlled substance reports</td>
</tr>
</tbody>
</table>

Notes:
1. Expected to change prior to 2014 with the introduction of controlled substances.
2. APRN (nurse) prescribers require controlled setting.
3. Controlled substance reports can be released by the patient.
4. Controlled substance reports are maintained with the patient’s medical record.

---
Questions?