New Drug Update 2016: Community Focus
Brooke McComb, PharmD

Objectives:

1. Identify significant therapeutic agents that were granted U.S. Food and Drug Administration approval in the past year
2. Describe indications, doses, adverse effects, drug interactions and pertinent patient counseling points for recently approved medications
3. Discuss the clinical impact and potential role in therapy of recently approved medications

Overview of 2015

- Increase in number of drug approvals
  - 45 new molecular entities approved
  - Average of 28 drugs approved per year since 2006
  - Applications for drug approvals remain steady

- Many noteworthy drug approvals
  - 16 of 45 were "first-in-class" including:
    - Bridion: To reverse post-surgical neuromuscular blockade
    - Ibrance: To treat advanced (metastatic) breast cancer
    - Praxbind: To reverse adverse anticoagulant effects caused by dabigatran
  - 21 of 45 were orphan drug approvals including:
    - Kanuma: To treat lysosomal acid lipase deficiency
    - Orkambi: To treat cystic fibrosis
    - Strensiq: Long-term enzyme replacement for infantile and juvenile hypophosphatemia
    - Unituxin: To treat pediatric patients with high-risk neuroblastoma
    - Xuriden: To treat patients with hereditary orotic aciduria
  - Variety of other impactful drugs

- Expedited drug approvals
  - 14 drugs were designated as Fast Track
  - 10 drugs were designated as Breakthrough therapies
  - 24 drugs were designated for Priority Review
  - 6 drugs were approved under FDA’s Accelerated Approval program
  - Total of 27 drugs approved in one or more expedited categories

- Other Statistics
  - 39 drugs were approved on First Cycle
  - 29 drugs were approved first in the United States before any other country
New Molecular Entities with a Community Focus

- **Savaysa (edoxaban)**
  - **Indication:** (1) To reduce the risk of stroke and systemic embolism in patients with nonvalvular atrial fibrillation. (2) For the treatment of deep vein thrombosis and pulmonary embolism following 5-10 days of initial parenteral anticoagulant therapy.
  - **Dose:** 60mg orally once daily
  - **Black Box Warning:** Reduced efficacy in nonvalvular atrial fibrillation with CrCl > 95 mL/min, premature discontinuation increases risk of ischemic events, spinal/epidural hematoma
  - **Adverse Reactions:** bleeding, anemia, rash, abnormal liver function tests
  - **Drug Interactions:** anticoagulants and rifampin

- **Cosentyx (secukinumab)**
  - **Indication:** For the treatment of moderate to severe plaque psoriasis (PP), active psoriatic arthritis (PA), or active ankylosing spondylitis (AS)
  - **Dose:**
    - PP = 300mg subcutaneously weekly for 4 weeks, then 300mg every 4 weeks
    - PA/AS = 150 mg subcutaneously weekly for 4 weeks, then 150 mg every 4 weeks
  - **Adverse Reactions:** Infections, nasopharyngitis, diarrhea
  - **Drug Interactions:** Live vaccines

- **Natpara (parathyroid hormone)**
  - **Indication:** To control hypocalcemia in patients with hypoparathyroidism
  - **Dose:** 50 mcg injected once daily in thigh
  - **Black Box Warning:** Increased risk of osteosarcoma
  - **Adverse Reactions:** Paresthesia, hypocalcemia, headache, hypercalcemia, nausea, hypoesthesia, diarrhea, vomiting, arthralgia, hypercalciriua, pain in extremity
  - **Drug Interactions:** Digoxin

- **Corlanor (ivabradine)**
  - **Indication:** To reduce the risk of hospitalization for worsening heart failure in patients with stable symptomatic chronic heart failure with left ventricular ejection fraction <35%, who are in sinus rhythm with resting heart rate > 70 beats per minute and either are on maximally tolerated doses of beta blockers or have a contraindication to beta-blocker use.
  - **Dose:** 5 mg orally twice daily
  - **Adverse Reactions:** bradycardia, hypertension, atrial fibrillation, and luminous phenomena
  - **Drug Interactions:** CYP3A4 inhibitors/inducers, negative chronotropes, pacemakers

- **Kybella (deoxycholic acid)**
  - **Indication:** For the improvement in the appearance of moderate to severe convexity or fullness associated with submental fat in adults
  - **Dose:** 0.2 mL injections spaced 1-cm apart until all sites complete (maximum of 10mL)
  - **Adverse Reactions (>20%):** injection site edema/swelling, hematoma, pain, numbness, erythema, induration
Viberzi (eluxadoline)\textsuperscript{7}
- **Indication:** For the treatment of irritable bowel syndrome with diarrhea
- **Dose:** 100 mg orally twice daily with food
- **Adverse Reactions:** constipation, nausea, abdominal pain
- **Drug Interactions:** OATP1B1 Inhibitors, Strong CYP Inhibitors, Drugs that Cause Constipation, OATP1B1 and BCRP Substrates, CYP3A4 Substrates with Narrow Therapeutic Index

Entresto (sacubitril/valsartan)\textsuperscript{8}
- **Indication:** To 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
- **Dose:** Starting = 49/51 mg orally twice daily; Target = 97/103 mg orally twice daily
- **Black Box:** Pregnancy
- **Adverse Reactions:** Hypotension, hyperkalemia, cough, dizziness, renal failure
- **Drug Interactions:** Dual blockage of the renin-angiotensin system, Potassium-sparing diuretics, NSAIDs, Lithium

Rexulti (brexpiprazole)\textsuperscript{9}
- **Indication:** For the treatment of schizophrenia and adjunctive therapy to antidepressants for the treatment of major depressive disorder
- **Dose:** Starting = 0.5 to 1 mg by mouth daily; Recommended = 2 to 4 mg by mouth daily
- **Black Box Warning:** Increased risk of suicidal thoughts and behaviors, elderly with dementia-related psychosis are at increased risk of death, safety not known in pediatrics
- **Adverse Reactions:** Metabolic changes, akathesia, leukopenia, neutropenia, agranulocytosis
- **Drug Interactions:** CYP2D6 inhibitors, CYP3A4 Inhibitors/Inducers

Praluent (alirocumab)\textsuperscript{10}
- **Indication:** For the treatment of heterozygous familial hypercholesterolemia or clinical atherosclerotic cardiovascular disease
  - Adjunct to diet & maximally tolerated statin therapy
  - The effect on cardiovascular morbidity and mortality has not been determined
- **Dose:** 75 mg subcutaneously every 2 weeks
- **Adverse Reactions:** Nasopharyngitis, injection site reactions, influenza

Addyi (flibanserin)\textsuperscript{11}
- **Indication:** For the treatment of premenopausal women with acquired, generalized hypoactive disorder as characterized by low sexual desire
- **Dose:** 100 mg orally once daily at bedtime
- **Black Box Warning:** Alcohol, CYP3A4 inhibitors, hepatic impairment
- **Adverse Reactions:** Dizziness, somnolence, nausea, fatigue, insomnia, and dry mouth
- **Drug Interactions:** Oral contraceptives, weak CYP3A4 inhibitors, strong CYP2C19 inhibitors, CYP3A4 inducers, Digoxin
- Repatha (evolocumab)\textsuperscript{12}
  - Indication: For the treatment of adults with heterozygous familial hypercholesterolemia, clinical atherosclerotic cardiovascular disease, or patients with homozygous familial hypercholesterolemia, who require additional lowering of low density lipoprotein cholesterol
    - Adjunct to diet & maximally tolerated statin therapy
    - The effect on cardiovascular morbidity and mortality has not been determined
  - Dose: 140 mg subcutaneous every 2 weeks or 420 mg subcutaneous every month
  - Adverse Reactions: Nasopharyngitis, upper respiratory tract infection, influenza, back pain, injection site reactions

- Vraylar (cariprazine)\textsuperscript{13}
  - Indication: For the treatment of schizophrenia and acute treatment of manic or mixed episodes associated with bipolar I disorder
  - Dose: 1.5 to 6 mg orally once daily with or without food
  - Black Box Warning: Dementia-related psychosis
  - Adverse Reactions: Extrapyramidal symptoms, akathisia, dyspepsia, vomiting, somnolence, restlessness
  - Drug Interactions: CYP3A4 inhibitors/inducers

- Tresiba (insulin degludec injection)\textsuperscript{14}
  - Indication: To improve glycemic control in patients with diabetes mellitus
  - Dose: Individualized based on insulin needs. Both U-100 and U-200 available.
  - Adverse Reactions: Hypoglycemia, allergic reactions, injection site reactions, lipodystrophy, pruritis, rash, edema, weight gain
  - Drug Interactions: Drugs that affect glucose metabolism, anti-adrenergic drugs

- Aristada (aripiprazole lauroxil)\textsuperscript{15}
  - Indication: For the treatment of schizophrenia
  - Dose: 441, 662, or 882 mg injected intramuscularly every 4-6 weeks
  - Black Box Warning: Dementia-related psychosis
  - Adverse Reactions: Akathisia, metabolic changes, leukopenia, orthostatic hypotension
  - Drug Interactions: CYP3A4 inducers/inhibitors, benzodiazepines, antihypertensives

- Nucala (mepolizumab)\textsuperscript{16}
  - Indication: For add-on maintenance treatment of patients with severe asthma aged 12 years and older, and with an eosinophilic phenotype
  - Dose: 100 mg subcutaneously every 4 weeks
  - Adverse Reactions: Headache, injection site reaction, back pain, and fatigue

- Uptravi (selexipag)\textsuperscript{17}
  - Indication: For the treatment of pulmonary arterial hypertension
  - Dose: Starting = 200 mcg orally twice daily; Maximum = 1600 mcg orally twice daily
  - Adverse Reactions: Headache, diarrhea, jaw pain, nausea, myalgia, vomiting, pain in extremity, flushing
  - Drug Interactions: Strong CYP2C8 Inhibitors
• Zurampic (lesinurad)\textsuperscript{18}
  
  o Indication: For the treatment of hyperuricemia associated with gout in patients who have not achieved target serum uric acid levels with a xanthine oxidase inhibitor alone
  
  o Dose: 200 mg orally daily with a xanthine oxidase inhibitor
  
  o Black Box Warning: Acute renal failure
  
  o Adverse Reactions: Headache, influenza, blood creatinine increase, gastroesophageal reflux
  
  o Drug Interactions: CYP2C9 Inhibitors, CYP3A4 substrates

Relevant Biological License Application Approvals\textsuperscript{19}

• Bexsero (meningococcal group B vaccine)
  
  o Active immunization to prevent invasive disease caused by Neisseria meningitis serotype B in individuals 10 through 25 years of age
  
  o Two intramuscular injections at least a month a part

• Quadracel (DTaP and inactivated poliovirus vaccine)
  
  o Indication: Active immunization against diphtheria, tetanus, pertussis, and poliomyelitis in children 4 through 6 years of age
  
  o Single intramuscular injection

• Fluad (influenza vaccine, adjuvanted)
  
  o Indication: Active immunization of persons 65 years of age and older against influenza disease caused by influenza virus subtypes A and B contained in the vaccine
  
  o Single intramuscular injection

Resources: