New Drug Update 2017
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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 2016
- Decrease in number of drug approvals
  - 22 new molecular entities approved in 2016
  - Average of 30 drugs approved annually from 2007 to 2015
  - Applications for drug approvals remain steady
- Many noteworthy drug approvals
  - Overall implications for positive impact on public health
  - 8 of 22 were “first-in-class” including:
    - Defitelio: to treat adults and children who develop hepatic veno-occlusive disease with additional kidney and lung abnormalities
    - Zinbryta: to treat multiple sclerosis
  - 9 of 22 were orphan drug approvals including:
    - Exondys 51: to treat patients with Duchenne muscular dystrophy
    - Spinraza: for treatment of patients with spinal muscular atrophy
  - Variety of other impactful drugs
- Expedited drug approvals
  - 8 drugs were designated as Fast Track
  - 7 drugs were designated as Breakthrough therapies
  - 15 drugs were designated for Priority Review
  - 6 drugs were approved under FDA’s Accelerated Approval program
  - Total of 16 drugs approved in one or more expedited categories
- Other Statistics
  - 21 drugs were approved within the Prescription Drug User Fee Act (PUDFA) goal dates
  - 21 drugs were approved on First Cycle
  - 19 drugs were approved first in the United States before any other country

New Molecular Entities

Hepatitis C
- ZEPATIERTM (elbasivir & grazoprevir)²
  - Indication: Treatment of chronic HCV genotype 1 or 4 infection in adults
  - Dose: 1 tablet (50mg/100mg) daily, without regard to food
  - Contraindications: Moderate or severe hepatic impairment (Child Pugh B or C), OATP1B1/3 inhibitors, strong CYP3A inhibitors, efavirenz
  - Adverse Reactions: fatigue, headache, insomnia and diarrhea
- **EPCLUSA® (sofosbuvir & velpatasvir)**
  - Indication: treatment of adult patients with chronic HCV genotypes 1, 2, 3, 4, 5 or 6 infections
    - Without cirrhosis or with compensated cirrhosis
    - With decompensated cirrhosis in combination with ribavirin
  - Dose: 1 tablet (400mg/100mg) daily, without regard to food
  - Drug Interactions: P-gp inducers, potent CYP 2B6, 2C8 and 3A4 inducers, antacids, rosuvastatin and atorvastatin
  - Adverse Reactions: headache and fatigue

**Asthma**

- **CINQAIR® (reslizumab)**
  - Indication: add-on maintenance treatment of patients 18 years or older with severe asthma with an eosinophilic phenotype
  - Dose: 3mg/kg IV infusion over 20-50 minutes every 4 weeks
  - Black Box Warning: anaphylaxis
  - Adverse Reactions: oropharyngeal pain, CPK elevations, muscle-related adverse reactions
  - Drug Interactions: no drug interaction studies have been conducted

**Kidney/Liver**

- **DEFITELIO® (defibrotide sodium)**
  - Indication: treatment of adult and pediatric patients with hepatic veno-occlusive disease with renal or pulmonary dysfunction following hematopoietic stem-cell transplantation
  - Dose: 6.26mg/kg every 6 hours as a 2-hour IV infusion for 21-60 days
  - Contraindications: concomitant administration of systemic anticoagulant or fibrinolytic therapy
  - Adverse Reactions: hypotension, nausea, vomiting, diarrhea, epistaxis

- **OCALIVA™ (obeticholic acid)**
  - Indication: treatment of primary biliary cholangitis in combination with ursodeoxycholic acid (UDCA) in adults with inadequate response to UDCA or as monotherapy in adults unable to tolerate UDCA
  - Dose: 5mg daily, may be increased after 3 months to 10mg daily
  - Adverse Reactions: pruritus, fatigue, abdominal pain and discomfort, rash, arthralgia, reduction in HDL-C
  - Drug Interactions: bile acid binding resins, warfarin, CYP1A2 substrates with narrow therapeutic index

**Neurologic Disorders**

- **BRIVIACT® (brivaracetam)**
  - Indication: adjunctive therapy in the treatment of seizures in patients 16 years of age and older with epilepsy
  - Dose: 50 mg twice daily but may be decreased to 25 mg or increased to 100 mg twice daily
  - Adverse Reactions: suicidal behavior and ideation, somnolence/sedation, dizziness, fatigue, irritability, nausea/vomiting, hematologic abnormalities
  - Drug Interactions: Rifampin, carbamazepine, phenytoin, levetiracetam

- **NUPLAZID™ (pimvanserin)**
  - Indication: to treat hallucinations and delusions associated with Parkinson’s disease psychosis
  - Dose: 34 mg daily taken in two 17 mg tablets by mouth once daily
  - Black Box Warning: Increased mortality in elderly patients with dementia-related psychosis
  - Adverse Reactions: peripheral edema, confusional state, nausea, hallucination
  - Drug Interactions: QT Interval Prolongation, Strong CYP3A4 inhibitors/inducers
• ZINBRYTA™ (daclizumab)9
  o Indication: to treat adult patients with relapsing forms of multiple sclerosis (reserved for patients who had an inadequate response to two or more drugs indicated for the treatment of MS).
  o Dose: 150 mg subcutaneously once monthly
  o Black Box Warning: hepatic injury including autoimmune hepatitis and other immune-mediated disorders
  o Adverse Reaction: nasopharyngitis, upper respiratory tract infection, rash, influenza, dermatitis, oropharyngeal pain, bronchitis, eczema, lymphadenopathy, increased ALT
  o Drug Interactions: hepatotoxic drugs

Skin Disorders
• TALTZ™ (ixekizumab)10
  o Indication: to treat patients with moderate-to-severe plaque psoriasis who are candidates for systemic therapy or phototherapy.
  o Dose: 160 mg subcutaneously once weekly (week 0), followed by 80 mg every two weeks for 12 weeks, then 80 mg every 4 weeks.
  o Adverse Reactions: injection site reactions, upper respiratory tract infections, nausea, tinea infections
  o Drug Interactions: live vaccines, cytochrome P450 substrates

• EUCRISA™ (crisaborole)11
  o Indication: to topically treat mild to moderate atopic dermatitis in patients 2 years of age and older
  o Dose: Apply to affected area twice daily (for topical use only; not for ophthalmic, oral, or intravaginal use)
  o Adverse Reactions: application site pain

Infectious Diseases
• ANTHIM™ (obiltoxaximab)12
  o Indication:
    ▪ Treatment of inhalational anthrax due to *B. anthracis* in combination with appropriate antibacterial drugs in adult and pediatric patients
    ▪ Prophylaxis of inhalational anthrax when alternative therapies are unavailable or inappropriate
  o Dose: 16mg/kg administered IV over 90 minutes
  o Adverse Reactions: hypersensitivity reactions (patients must be pre-treated with diphenhydramine and monitored during infusion)

• ZINPLAVA® (bezlotoxumab)13
  o Indication: to reduce recurrence of *C. difficile* infection (CDI) in patients 18 years and older who are receiving antibacterial drug treatment for CDI and are at high risk for CDI recurrence
  o Dose: 10mg/kg single dose IV infusion over 60 minutes
  o Adverse Reactions: nausea, pyrexia and headache
  o Warning: increased risk of experiencing heart failure, especially in patients with a history of CHF
  o Drug Interactions: none (metabolized by catabolism)
Diagnostic Agents

- **AXUMINTM (fluciclovine F 18)**14
  - Indication: for positron emission tomography (PET) in men with suspected prostate cancer recurrence based on elevated blood prostate specific antigen (PSA) levels following prior treatment
  - Dose: 370MBq (10 mCi) administered as an IV bolus
  - Adverse Reactions: Injection site pain, injection site erythema and dysgeusia

- **NETSPOTTM (gallium Ga 68 dotate)**15
  - Indication: for use with positron emission tomography (PET) for localization of somatostatin receptor positive neuroendocrine tumors (NETs) in adult and pediatric patients
  - Dose: 2Mbq/kg of body weight (0.054 mCi/kg) up to 200MBq (5.4 mCi) as an IV bolus
  - Adverse Reactions: No serious adverse reactions identified

Muscular Disorders

- **EXONDYS 51TM (eteplirsen)**16
  - Indication: treatment of Duchenne muscular dystrophy (DMD) in patients who have a confirmed mutation of the DMD gene that is amenable to exon 51 skipping.
  - Dose: 30mg/kg once weekly as a 35-60 minute IV infusion
  - Adverse Reactions: balance disorder, contact dermatitis, vomiting
  - Drug Interactions: based on in vitro data, expected to have low potential for drug-drug interaction in humans

- **SPINRAZATM (nusinersin)**17
  - Indication: treatment of spinal muscular atrophy in pediatric and adult patients
  - Dose: 12mg intrathecally
    - Begin with 4 loading doses: Day 1, day 14 and day 28, then 30 days after the third dose
    - Maintenance dose should be administered every 4 months thereafter
  - Warnings: thrombocytopenia and coagulation abnormalities, renal toxicity
  - Adverse Reactions: headache, back pain, post-lumbar puncture syndrome

Oncology

- **VENCLEXTATM (venetoclax)**18
  - Indication: to treat patients with chronic lymphocytic leukemia (CLL) with 17p deletion who have received at least one prior therapy (approved under accelerated approval based on response rate; continued approval may be contingent upon verification).
  - Dose: 20 mg by mouth once daily for 7 days; titrated up weekly to the recommended daily dose of 400 mg.
  - Adverse Reaction: Neutropenia, diarrhea, nausea, anemia, upper respiratory tract infection, thrombocytopenia, infection
  - Drug Interactions: moderate CYP3A inhibitors, strong or moderate CYP3A inducers, P-gp inhibitors, or narrow therapeutic index P-gp substrates

- **TECENTRIQ® (atezolizumab)**19
  - Indication: to treat patients with (1) locally advanced or metastatic urothelial carcinoma who have disease progression during or following platinum-containing chemotherapy and have disease progression within 12 months of neoadjuvant treatment with platinum-containing chemotherapy or (2) metastatic non-small cell lung cancer who have disease progression during or following platinum-containing chemotherapy.
  - Dose: 1200 mg as an intravenous infusion over 60 minutes every 3 weeks
- **LARTRUVO** (olaratumab): Indication: to treat adults with soft tissue sarcoma (STS) with a histologic subtype for which an anthracycline-containing regimen and which is not amenable to curative treatment with radiotherapy or surgery. Dose: 15 mg/kg as an intravenous infusion over 60 minutes on Days 1 and 8 of each 21-day cycle until disease progression or unacceptable toxicity. For the first 8 cycles, Lartruvo is administered with doxorubicin. Prior to Lartruvo on Day 1 of cycle 1, premedicate with diphenhydramine and dexamethasone intravenously. Do not administer as an intravenous push or bolus. Adverse Reactions: nausea, fatigue, musculoskeletal pain, mucositis, alopecia, vomiting, diarrhea, decreased appetite, abdominal pain, neuropathy, headache.

- **RUBRACA** (rucaparib): Indication: to treat patients with deleterious BRCA mutation (germline and/or somatic) associated advanced ovarian cancer who have been treated with two or more chemotherapies. Dose: 600 mg by mouth twice daily until disease progression or unacceptable toxicity. Adverse Reactions: nausea, fatigue, vomiting, anemia, abdominal pain, dysgeusia, constipation, increased appetite, diarrhea, thrombocytopenia, dyspnea, laboratory abnormalities.

### Ocular

- **XIIDRA** (lifitegrast ophthalmic solution): Indication: to treat the signs and symptoms of dry eye disease (DED). Dose: 1 drop in each eye twice daily (approximately 12 hours apart). Adverse Reactions: instillation site irritation, dysgeusia and decreased visual acuity.

### Diabetes

- **ADLYXIN** (lixisenatide): Indication: to improve glycemic control in patients with type 2 diabetes mellitus in adjunct to diet and exercise. Dose: 10 mcg subcutaneously once daily for 14 days, then increase to 20 mcg once daily. Adverse Reactions: nausea, vomiting, headache, diarrhea, dizziness, hypoglycemia. Drug Interactions: delayed gastric emptying effects on oral medications, dosage adjustment of sulfonylurea or basal insulin with concomitant use.

### References: