New Drug Update

Greg Bradford, PharmD
Clinical Pharmacy Specialist
Shelby Baptist Medical Center
I have no actual or potential conflicts of interest relevant to this activity.

I know enough to know that I don't know enough.
Objectives

- Briefly review new drugs approved in 2016
- Recognize new drugs to date in 2017
- Discuss new drugs which may impact hospital pharmacy practice
- Identify any drug label changes or drug use trends which may impact hospital pharmacy practice
Drug Approvals

CDER New Molecular Entity (NME) and New Biologic License Application (BLA) Filings and Approvals

https://www.fda.gov/drugs/developmentapprovalprocess/druginnovation/ucm534863.htm
Last accessed April 28, 2017
<table>
<thead>
<tr>
<th>Drug name</th>
<th>Active ingredient</th>
<th>Route</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Defitelio</td>
<td>Defibrotide sodium</td>
<td>IV infusion</td>
<td>To treat adults and children who develop hepatic veno-occlusive disease with additional kidney or lung abnormalities after receiving hematopoietic stem cell transplant</td>
</tr>
<tr>
<td>Exondys 51</td>
<td>Eteplirsen</td>
<td>IV infusion</td>
<td>To treat Duchenne muscular dystrophy</td>
</tr>
<tr>
<td>Ocaliva</td>
<td>Obeticholic acid</td>
<td>Oral</td>
<td>To treat primary biliary cirrhosis</td>
</tr>
<tr>
<td>Spinraza</td>
<td>Nusinersen</td>
<td>Intrathecal</td>
<td>To treat children and adults with spinal muscular atrophy</td>
</tr>
<tr>
<td>Venclexta</td>
<td>Venetoclax</td>
<td>Oral</td>
<td>For chronic lymphocytic leukemia in patients with a specific chromosomal abnormality</td>
</tr>
<tr>
<td>Xiidra</td>
<td>Lifitegrast</td>
<td>Ophthalmic</td>
<td>To treat signs and symptoms of dry eye disease</td>
</tr>
<tr>
<td>Zinbryta</td>
<td>Daclizumab</td>
<td>SQ injection</td>
<td>To treat multiple sclerosis</td>
</tr>
<tr>
<td>Zinplava</td>
<td>Bezlotoxumab</td>
<td>IV infusion</td>
<td>To reduce the occurrence of Clostridium difficile infection in patients aged 18 years or older</td>
</tr>
</tbody>
</table>
**Bezlotoxumab (Zinplava™)**

**Mechanism:**

Monoclonal antibody which binds to *Clostridium difficile* toxin B

**Indication:**

To reduce recurrence of *Clostridium difficile* infection (CDI) in patients ≥ 18 years of age who are receiving antibacterial drug treatment of CDI & are at high risk for CDI recurrence

**Limitations:**

Not indicated for treatment of CDI

Only can be used in conjunction w/ antibacterial treatment of CDI
Monoclonal Antibodies for *C. difficile* Therapy

- Two global, Phase 3, double blind studies (MODIFY 1 & 2)
- Primary endpoint: *C. difficile* recurrence through week 12
- All patients received 10-14 days of standard of care antibiotics
  - Oral metronidazole (48%)
  - Oral vancomycin +/- IV metronidazole (48%)
  - Oral fidoxamicin +/- IV metronidazole (4%)

- **Study arms included:**
  - Bezlotoxumab monotherapy
  - Actoxumab monotherapy (MODIFY 1 only)- stopped early for efficacy and safety reasons
  - Bezlotoxumab and actoxumab infusions
  - Placebo

- **Results:**
  - MODIFY 1- bezlotoxumab 17.4% (p=0.0003); bezlotoxumab + actoxumab 15.9% (p<0.0001); placebo 27.6%
  - MODIFY 2- bezlotoxumab 15.7% (p=0.0003); bezlotoxumab + actoxumab 14.9% (p<0.0001); placebo 25.7%
Bezlotoxumab (Zinplava™)

Dosing/administration:

10 mg/kg IV as a single infusion over 60 minutes
Administer via a low-protein binding 0.2 - 5 micron in-line or add-on filter

Adverse Effects:
Nausea, pyrexia, headache

Warnings:
Heart Failure exacerbation
### 2016 Notables

#### Hepatitis C Breakthroughs

<table>
<thead>
<tr>
<th>Drug</th>
<th>HCV Genotypes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zepatier (elbasvir; grazoprevir)</td>
<td>1 and 4</td>
</tr>
<tr>
<td>Epclusa (sofosbuvir; velpatasvir)</td>
<td>All 6 major forms of HCV</td>
</tr>
</tbody>
</table>

#### -mabs

<table>
<thead>
<tr>
<th>Drug</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anthim (obiltoxaximab)</td>
<td>Add on to treat inhalational anthrax</td>
</tr>
<tr>
<td>Taltz (ixekizumab)</td>
<td>Treat moderate to severe plaque psoriasis</td>
</tr>
<tr>
<td>Cinqair (reslizumab)</td>
<td>Treat severe asthma</td>
</tr>
<tr>
<td>Tecentriq (atezolizumab)</td>
<td>Treat urothelial carcinoma</td>
</tr>
<tr>
<td>Lartruvo (olaratumab)</td>
<td>Treat adults with certain types of soft tissue sarcoma</td>
</tr>
</tbody>
</table>

#### Honorable Mention

<table>
<thead>
<tr>
<th>Drug</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Briviact (brivaracetam)</td>
<td>Partial onset seizures ≥ 16 years old</td>
</tr>
<tr>
<td>Nuplazid (pimavanserin)</td>
<td>Treat hallucinations and delusions associated with psychosis experienced by some with Parkinson’s disease</td>
</tr>
</tbody>
</table>
Biosimilars

- Inflectra (infliximab-dyyb)
- Erelzi (etanercept-szzs)
- Amjevita (adalimumab-atto)
Significant New Dosage Forms

- Injectable carbamazepine (Carnexiv®)
- Effervescent tablet acetylcysteine (Cetylev®)
- New oral solutions
  - Enalapril (Epaned®)
  - Lisinopril (Qbrelis®)
- Subdermal implant buprenorphine (Probuphine®)
- Tablet form methylnaltrexone (Relistor®)
Long-acting Insulin and Glucagon-Like Peptide-1 (GLP-1) Receptor Agonists

Insulin glargine/lixisenatide (Soliqua®)
- Type 2 DM inadequately controlled on < 60 units of basal insulin daily or lixisenatide
- Dosing:
  - Initially 15 units (insulin glargine 15 units/lixisenatide 5 mcg) or 30 units (insulin glargine 30 units/lixisenatide 10 mcg)/day
  - Max is 60 units (insulin glargine 60 units/lixisenatide 20 mcg)/day
  - Not recommended in CrCl < 15
- Adverse drug reactions:
  - Nausea, headache
  - Pancreatitis
- Drug Interactions: contraceptives

Insulin degludec/liraglutide (Xultophy®)
- Type 2 DM inadequately controlled on < 50 units of basal insulin daily or liraglutide (less than or equal to 1.8 mg daily)
- Dosing:
  - Initially 16 units insulin and 0.58 mg liraglutide/day
  - Max is 50 units insulin and 1.8 mg liraglutide/day
  - No renal adjustments
- Adverse drug reactions:
  - Nausea, diarrhea
  - Risk of thyroid C-cell tumors
Long-acting Insulin & GLP-1 Receptor Agonists

Advantages
• Less hypoglycemia
• Weight neutral/loss
• Single injection
• Associated with lower CVD event rate and mortality in patients with CVD (liraglutide LEADER*)
• A1c reduction up to 2%

Disadvantages
• GI side effects
• ? Pancreatitis
• Injectable pen only
• Costs

### 2017 new drugs to date

<table>
<thead>
<tr>
<th>Brand</th>
<th>Generic</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Radicava</td>
<td>edaravone</td>
<td>Amyotrophic lateral sclerosis (ALS)</td>
</tr>
<tr>
<td>Imfinzi</td>
<td>durvalumab</td>
<td>Locally advanced or metastatic urothelial carcinoma</td>
</tr>
<tr>
<td>Tymlos</td>
<td>abaloparatide</td>
<td>Osteoporosis in postmenopausal women at high risk of fracture or those who have failed other therapies</td>
</tr>
<tr>
<td>Rydapt</td>
<td>midostaurin</td>
<td>Acute myeloid leukemia</td>
</tr>
<tr>
<td>Alunbrig</td>
<td>brigatinib</td>
<td>Anaplastic lymphoma kinase (ALK)-positive metastatic non-small cell lung cancer (NSCLC) who have progressed on or are intolerant to crizotinib</td>
</tr>
<tr>
<td>Brineura</td>
<td>cerliponase alfa</td>
<td>Specific form of Batten disease</td>
</tr>
<tr>
<td>Ingrezza</td>
<td>valbenazine</td>
<td>Tardive dyskinesia</td>
</tr>
<tr>
<td>Austedo</td>
<td>deutetrabenazine</td>
<td>Chorea associated with Huntington’s disease</td>
</tr>
<tr>
<td>Ocrevus</td>
<td>ocrelizumab</td>
<td>Relapsing and primary progressive forms of multiple sclerosis</td>
</tr>
<tr>
<td>Dupixent</td>
<td>dupilumab</td>
<td>Moderate-to-severe eczema (atopic dermatitis)</td>
</tr>
</tbody>
</table>
## 2017 new drugs to date

<table>
<thead>
<tr>
<th>Brand</th>
<th>Generic</th>
<th>indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zejula</td>
<td>niraparib</td>
<td>Maintenance treatment for recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancers</td>
</tr>
<tr>
<td>Symproic</td>
<td>naldemedine</td>
<td>Opioid-induced constipation</td>
</tr>
<tr>
<td>Bavencio</td>
<td>avelumab</td>
<td>Metastatic Merkel cell carcinoma</td>
</tr>
<tr>
<td>Xadago</td>
<td>safinamide</td>
<td>Parkinson’s disease</td>
</tr>
<tr>
<td>Kisqali</td>
<td>ribociclib</td>
<td>Postmenopausal women with a type of advanced breast cancer</td>
</tr>
<tr>
<td>Xermelo</td>
<td>telotristat ethyl</td>
<td>Carcinoid syndrome diarrhea</td>
</tr>
<tr>
<td>Siliq</td>
<td>brodalumab</td>
<td>Moderate-to-severe plaque psoriasis</td>
</tr>
<tr>
<td>Emflaza</td>
<td>deflazacort</td>
<td>Patients 5 yrs old and older with Duchenne muscular dystrophy</td>
</tr>
<tr>
<td><strong>Parsabiv</strong></td>
<td><strong>etelcalcitide</strong></td>
<td><strong>Secondary hyperparathyroidism in adults with chronic kidney disease undergoing dialysis</strong></td>
</tr>
<tr>
<td>Trulance</td>
<td>plecanatide</td>
<td>Chronic idiopathic constipation</td>
</tr>
</tbody>
</table>
**Etelcalcitide (Parsabiv®)**

**Mechanism:** binds to the calcium-sensing receptor and enhances activation of the receptor by circulating calcium, resulting in decreased parathyroid hormone (PTH) secretion.

**Pharmacokinetics:** 3-4 day half-life in CKD patients on HD; effects on PTH seen within 30 minutes of administration; steady state reached ~7-8 weeks

**Dosing:** 5 mg IV bolus at the end of hemodialysis session, 3 times/week
   Adjust q 4 weeks to maintain target PTH levels. Max dose is 15 mg.

**ADR:** hypocalcemia; muscle spasms; QTc prolongation; seizures

**Monitoring:** PTH and serum calcium every 4 weeks
Two 6-months, double-blind, randomized, placebo-controlled trials.

Primary endpoint: proportion of patients who achieved a > 30% reduction from baseline in mean PTH

Study arms (vitamin D &/or phosphate binders allowed for both):

- etelcalcitide 5 mg TIW at the end of hemodialysis and titrated every 4 weeks through week 17 to a max dose of 15 mg three times per week
- Placebo

Results:

- 78% etelcalcitide patients achieved a > 30% reduction from baseline PTH
- 11.1% placebo achieved primary endpoint
### Calcimimetics

<table>
<thead>
<tr>
<th></th>
<th>Cinacalcet (Sensipar®)</th>
<th>Etelcalcitide (Parsabiv®)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dosage Form</strong></td>
<td>PO</td>
<td>IV</td>
</tr>
<tr>
<td><strong>Indication</strong></td>
<td>• Primary hyperparathyroidism, severe hypercalcemia</td>
<td>• Secondary hyperparathyroidism, CKD patients on HD</td>
</tr>
<tr>
<td></td>
<td>• Secondary hyperparathyroidism, CKD patients on HD</td>
<td>• Secondary hyperparathyroidism, CKD patients on HD</td>
</tr>
<tr>
<td></td>
<td>• Hypercalcemia in patients with parathyroid carcinoma</td>
<td>Unknown- expected to be comparable to cinacalcet</td>
</tr>
<tr>
<td><strong>Cost (30 day)</strong></td>
<td>~$1,000</td>
<td>Unknown- expected to be comparable to cinacalcet</td>
</tr>
</tbody>
</table>
Mechanism:  
dapagliflozin- sodium-glucose cotransporter 2 (SGLT-2) inhibitor  
saxagliptin- dipeptidyl peptidase-4 (DPP-4) inhibitor  

Dosing:  
10 mg dapagliflozin and 5 mg saxagliptin PO once daily in the morning  
Do not initiate if eGFR is or persistently falls less than 60 ml/min/1.73 m²  

ADR:  
increased Scr, AKI; genitourinary infections; hypotension/hypovolemia; ketoacidosis  

Place in therapy:  
Added to metformin if A1c not at goal; initiated as dual therapy in patients with A1c > 9% who cannot tolerate metformin
Drug News

- Post marketing discoveries
- Antimicrobial Stewardship Initiative 2017
- Drug Prices
- Biosimilar Interchangeability
- USP 800
- Opioid Stewardship
True or False

Bezlotoxumab is a new antibiotic used in the treatment of *C difficile* in patients not responding to standard of care.
Which of the following is/are potential advantages of the new long acting insulin/GLP-1 receptor agonists combinations vs basal/bolus insulin?

A. Less hypoglycemia
B. Single injection
C. Weight loss/neutral
D. All of the above
Etelcalcitide is administered:

A. Daily via oral route
B. 3 times per week via oral route
C. 3 times per week IV at the end of HD session
D. 3 times per week IV before each HD session
Questions