Keeping Up-to-Date, with so Little Time: Newly Approved Medication Review

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Pharmacist Objectives

At the conclusion of this program, the pharmacist will be able to:

1. Identify new molecular and biological entities that entered the U.S. drug market in the past year (excluding diagnostic compounds)

2. Describe each agent's mechanism of action, dosage, adverse reactions, contraindications, and drug interaction profile

3. List patient counseling on special instructions and monitoring parameters for each agent

4. Identify molecular entities that have been approved as generic medications by the FDA in the past year
Technician Objectives

At the conclusion of this program, the technician will be able to:

1. Identify new molecular and biological entities that entered the U.S. drug market in the past year (excluding diagnostic compounds)

2. Describe each agent's mechanism of action, dosage, adverse reactions, contraindications, and drug interaction profile

3. List patient counseling on special instructions and monitoring parameters for each agent

4. Identify molecular entities that have been approved as generic medications by the FDA in the past year
How many new molecular entities were approved in 2016?

a) 22  
b) 27  
c) 41  
d) 45
What medical indication was ixekizumab approved for?

a) Plaque psoriasis
b) Type 2 Diabetes
c) Hyperlipidemia
d) Hepatitis C
What medical indication was valbenazine approved for?

a) Osteoporosis  
b) Bipolar disorder  
c) Tardive dyskinesia  
d) Opioid-induced constipation
Pre-Test Questions

What medical indication was plecanatide approved for?

a) Dermatitis
b) Constipation
c) Type 2 Diabetes
d) Multiple sclerosis
Keeping Up-to-Date, with so Little Time: Newly Approved Medication Review
Outline

- Newly approved medications
- New dosage formulations and combinations
- Recent generics
- Upcoming generics
- Products removed from market
CYP P450 Substrates

- **3A4 inhibitors:**
  - Amiodarone
  - Cimetidine
  - Clarithromycin
  - Diltiazem
  - Erythromycin
  - Grapefruit juice
  - Ketoconazole
  - Verapamil

- **3A4 inducers:**
  - Carbamazepine
  - Oxcarbazepine
  - Phenobarbital
  - Phenytoin
  - Pioglitazone
  - Rifampin
  - Topiramate
  - St. John’s wort

- **2D6 inhibitors:**
  - Amiodarone
  - Bupropion
  - Diphenhydramine
  - Fluoxetine
  - Haloperidol
  - Paroxetine
  - Terbinafine
  - Chloroquine

Lexi-Comp, Inc. (Lexi-Drugs®). Lexi-Comp, Inc.; August 17, 2017
To date in 2017 ➔ 28
Ixekizumab (Taltz®)
Eli Lilly

- **Indication:**
  - Indicated for adults with moderate-to-severe plaque psoriasis

- **Mechanism of action:**
  - Humanized monoclonal IgG4 antibody that targets interleukin-17A and neutralizes the proinflammatory effects of IL-17A
    - IL-17A is a naturally occurring cytokine that is involved in normal inflammatory and immune responses and plays a key role in the pathogenesis of plaque psoriasis

- **Dosage forms:**
  - Available as: SubQ injection 80mg/mL
    - Autoinjector or prefilled syringe

- **Administration**
  - Intended for use under the guidance and supervision of a physician

https://www.taltz.com/how-to-use-taltz.html

U.S. Food and Drug Administration, 2016,
http://uspl.lilly.com/taltz/taltz.html#pi
**Ixekizumab (Taltz®)**

**Eli Lilly**

- **Dosing**:
  - Week 0: 160 mg SC (two 80-mg injections), THEN
  - 80 mg SC q2wks at weeks 2, 4, 6, 8, 10, and 12, THEN
  - 80 mg SC q4wks

- **Dosing Considerations**
  - Evaluate patients for tuberculosis prior to initiating treatment

- **Contraindications**
  - Previous serious hypersensitivity reaction (eg, anaphylaxis) to drug or excipients

- **Precautions**
  - May increase the risk of infection
  - Serious hypersensitivity reactions reported
    - angioedema AND urticaria

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**Ixekizumab (Taltz®)**
Eli Lilly

- **Adverse Reactions**
  - Injection site reactions (17%)
  - Upper respiratory tract infections (14%)
  - Serious infections (3%)
  - Nausea (2%)
  - Tinea infections (2%)
  - Serious hypersensitivity reactions (<1%)

- **Drug Interactions**
  - Do NOT administer with live vaccines

U.S. Food and Drug Administration, 2016,
http://uspl.lilly.com/taltz/taltz.html#pi
Source: https://www.google.com/search?q=Taltz&source=lnms4NYD_1DM:
Brivaracetam (Briviact®)
UCB

- **Indication:**
  - Adjunctive therapy for partial-onset seizures

- **Mechanism of action:**
  - Exact mechanism unknown
    - Theory:
      - High and selective affinity for synaptic vesicle protein 2A in the brain
        » May contribute to the anticonvulsant effect

- **Dosing:**
  - Oral route
    - 50 mg PO BID
      - Titrate as needed from 25mg BID to 100mg BID
  - Injection
    - Used when PO is temporarily not feasible

- **Dosage forms & strengths:**
  - Tablet: 10mg, 25mg, 50mg, 75mg, 100mg
  - Oral solution: 10mg/mL
  - Injection: 50mg/5mL

Brivaracetam (Briviact®)

UCB

• Dosage modifications
  – Hepatic impairment
    • All stages:
      – starting dose 25 mg BID
      – not to exceed 75 mg BID
  – Renal impairment
    • ESRD undergoing dialysis: Not recommended

• Contraindications
  – Hypersensitivity; bronchospasms and angioedema

• Precautions
  – Increase the risk of suicidal behavior and ideation
  – Monitor for emergence or worsening of depression
  – Taper medication when discontinued
    • Increased risk of seizure frequency

U.S Food and Drug Administration, 2016,
https://www.briviact.com/briviact-Pl.pdf?v=1479491757
Brivaracetam (Briviact®)

UCB

- **Adverse Reactions**
  - Somnolence and sedation (16%)
  - Dizziness (12%)
  - Fatigue (9%)
  - Nausea and vomiting (5%)
  - Cerebellar coordination and balance disturbances (3%)
  - Irritability (3%)

- **Drug Interactions**
  - CYP2C19 substrates
    - Carbamazepine, phenobarbital, phenytoin,
    - Rifampin: increase dose by 100% (i.e. double dose)

- **Schedule under DEA review**

U.S Food and Drug Administration, 2016,
https://www.briviact.com/briviact-Pl.pdf?v=1479491757
Pimavanserin (Nuplazid™)
Acadia

• **Indication:**
  – Treatment of hallucinations and delusions associated with Parkinson disease psychosis

• **Mechanism of action:**
  – Selective serotonin inverse agonist and antagonist activity preferentially targeting 5-HT2A receptors believed to play an important role in psychosis

• **Dosing:**
  – 34 mg PO daily (2 – 17mg tablets)

U.S Food and Drug Administration, 2016,
Pimavanserin (Nuplazid™)
Acadia

- Contraindications
  - None

- Boxed Warning
  - Antipsychotic drugs increase the all-cause risk of death in elderly patients with dementia-related psychosis

- Precautions
  - QTc prolongation
  - Renal impairment
    - Mild-to-moderate (CrCl ≥30 mL/min): No dosage adjustment required
    - Severe (CrCl <30 mL/min): Not evaluated
  - Hepatic impairment
    - Not recommended (not evaluated)

U.S. Food and Drug Administration, 2016,
Pimavanserin (Nuplazid™)
Acadia

• Adverse Reactions
  – Nausea (7%)
  – Peripheral edema (7%)
  – Confusional state (6%)
  – Hallucinations (5%)
  – Constipation (4%)
  – Gait disturbance (2%)

• Drug Interactions
  – Co-administration with strong CYP3A4 inhibitors
    • Decrease dose to 17 mg PO daily
Reslizumab (Cinqair®)

Teva

- **Indication:**
  - Add-on maintenance treatment of patients with severe asthma aged ≥18 years with an eosinophilic phenotype

- **Mechanism of action:**
  - Interleukin-5 antagonist monoclonal antibody

- **Dosage form:**
  - IV solution
  - 100mg/10mL vial

- **Dosing:**
  - 3 mg/kg IV q4wk infused over 20-50 minutes

- **Limitations of use:**
  - Not indicated for treatment of other eosinophilic conditions or relief of acute bronchospasm

Reslizumab (Cinqair®)

Teva

• Contraindications
  – Known hypersensitivity to reslizumab or its excipients

• Boxed Warnings
  – Anaphylaxis occurred in 0.3% of patients in placebo-controlled studies
    • Discontinue immediately if the patient experiences anaphylaxis
      – Observe patient for 20 minutes post infusion

• Precautions
  – Should not be used to treat acute asthma symptoms or acute exacerbations
  – Do NOT administer as IV push or bolus
Reslizumab (Cinqair®)
Teva

• Adverse Reactions
  – Elevated CPK (14%)
  – Oropharyngeal pain (2.6%)
  – Myalgias (1%)
  – Anaphylaxis (0.3%)

• Administration
  – Should be administered in a healthcare setting by a healthcare professional prepared to manage anaphylaxis
Daclizumab (Zinbryta™)
Biogen

• **Indication:**
  – Indicated for adults with relapsing forms of multiple sclerosis (MS)

• **Mechanism of Action:**
  – Humanized monoclonal antibody that binds to the high-affinity interleukin-2 (IL-2) receptor subunit (CD25)
    • These subunits are expressed at high levels on T-cells that become abnormally activated in multiple sclerosis

• **Dosing:**
  – 150 mg SC once monthly

• **Place in therapy:**
  – Reserved for patients who have inadequate response to ≥2 other drugs for MS

U.S Food and Drug Administration, 2016,
Daclizumab (Zinbryta™)
Biogen

• **Boxed warnings:**
  – Can cause severe liver injury including life-threatening events, liver failure, and autoimmune hepatitis
  – Serious immune-mediated conditions were observed in 5% of treated patients
    • (eg, skin reactions, noninfectious colitis)

• **Contraindications:**
  – Preexisting hepatic disease or hepatic impairment
    • ALT or AST at least 2 x ULN

• **Precautions:**
  – Available only through a restricted access program
    • Risk Evaluation and Mitigation Strategy (REMS) called the ZINBRYTA REMS Program

U.S. Food and Drug Administration, 2016,
Daclizumab (Zinbryta™)

Biogen

• Adverse Reactions:
  – Immune-mediated disorders (28-32%)
  – Nasopharyngitis (25%)
  – Skin reactions (19%)
  – Upper respiratory tract infection (9-17%)
  – Rash (9-11%)

• Drug Interactions:
  – Hepatotoxic medications
  – Live vaccines are not recommended during treatment and up to 4 months after treatment

• Monitoring:
  – ALT/AST and bilirubin levels
    • Before initiating then monthly

U.S. Food and Drug Administration, 2016,
### Table 1: ZINBRYTA Treatment Modification for Liver Test Abnormalities

<table>
<thead>
<tr>
<th>Lab Value(s)</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALT or AST greater than 5 times ULN OR</td>
<td>• Interrupt ZINBRYTA therapy and investigate for other etiologies of abnormal lab value(s).</td>
</tr>
<tr>
<td>Total bilirubin greater than 2 times ULN OR</td>
<td>• If no other etiologies are identified, then discontinue ZINBRYTA.</td>
</tr>
<tr>
<td>ALT or AST greater than or equal to 3 but less than 5 times ULN and total bilirubin greater than 1.5 but less than 2 times ULN</td>
<td>• If other etiologies are identified, re-assess the overall risk-benefit profile of ZINBRYTA in the patient and consider whether to resume ZINBRYTA when both AST or ALT are less than 2 times ULN and total bilirubin is less than or equal to ULN.</td>
</tr>
</tbody>
</table>

In clinical trials, permanent discontinuation of therapy was required if the patient had liver test abnormalities resulting in suspension of study treatment for at least 8 consecutive weeks.

ULN = upper limit of normal
Cholera vaccine (Vaxchora™)

PaxVax

• Indication:
  – Indicated for cholera prevention for travelers ages 18 – 64 visiting areas with active cholera transmission
    • Only vaccine available to prevent cholera at this time

• Mechanism of Action:
  – Vaccine contains live attenuated cholera bacteria that replicate in the gastrointestinal tract of the recipient to provide immunity

• Dosing:
  • Single dose, live attenuated oral vaccine
  • Administered 10 days or more before travel
  • Duration of coverage is unknown
    – (3 – 6 months)

U.S. Food and Drug Administration, 2016,
https://www.paxvaxconnect.com/PDF/Vaxchora_Prescribing_Information.pdf
Cholera vaccine (Vaxchora™)
PaxVax

• Precautions:
  – Immunocompromised persons

• Adverse Reactions:
  – Mild headache (18.9%)
  – Mild tiredness (18.7%)
  – Mild nausea/vomiting (13.3%)
  – Mild abdominal pain (12.1%)
  – Moderate tiredness (12%)
  – Decreased appetite, mild (11.7%)

U.S Food and Drug Administration, 2016,
https://www.paxvaxconnect.com/PDF/Vaxchora_Prescribing_Information.pdf
Cholera vaccine (Vaxchora™)
PaxVax

Source:
http://www.who.int/gho/epidemic_diseases/cholera/epidemics/en/
Lixisenatide (Adlyxin™)
Sanofi

• Indication:
  – Indicated to improve glycemic control in adults with type 2 diabetes mellitus

• Mechanism of Action:
  – Incretin mimetic; glucagonlike peptide-1 (GLP-1) receptor agonist; increases glucose-dependent insulin release, decreases glucagon secretion, and slows gastric emptying

• Dosing:
  – Starting dose:
    • 10 mcg SC qDay for 14 days
  – Maintenance:
    • Increase dose to 20 mcg SC qDay starting on Day 15
  – Starter dose (green pen)
    • 50mcg/mL in 3mL prefilled pen (provides 14 doses of 10mcg/dose)
  – Maintenance dose (burgundy pen)
    • 100mcg/mL in 3 mL prefilled pen (provides 14 doses of 20mcg/dose)
Lixisenatide (Adlyxin™)
Sanofi
Lixisenatide (Adlyxin™)
Sanofi

- **Dosing considerations:**
  - Not a substitute for insulin
  - Not indicated for patients with type 1 DM
  - Do not used with short acting insulin (not studied)

- **Adverse Reactions:**
  - Nausea (25%)
  - Hypoglycemia
    - Coadministered with basal insulin +/- sulfonylurea (47.2%)
    - Coadministered with basal insulin +/- metformin (28.3%)
    - Coadministered with insulin glargine and metformin +/- thiazolidinedione (22%)
    - Coadministered with sulfonylurea +/- metformin (14.5%)
Drug Interactions:

- Lixisenatide delays gastric emptying, which may affect absorption of concomitantly administered oral medications.
- Medications with narrow therapeutic index or careful clinical monitoring should be used with caution.
- Oral contraceptives should be taken at least 1 hr before lixisenatide administration or 11 hr after lixisenatide.
Plecanatide (Trulance™)
Synergy Pharmaceuticals

• Indication:
  – chronic idiopathic constipation in adults

• Mechanism of action:
  – Guanylate cyclase C (GC-C) agonist
    • stimulates secretion of chloride and bicarbonate into the intestinal lumen → increased intestinal fluid and accelerated transit

• Dosing:
  – 3 mg PO qDay

U.S Food and Drug Administration, 2017,
Plecanatide (Trulance™)  
Synergy Pharmaceuticals

• Contraindications  
  – Children <6 years old  
    • Dehydration → death (mice)  
  – Known or suspected mechanical gastrointestinal obstruction

• Precautions  
  – Risk of serious dehydration in pediatric patients  
  – Diarrhea

U.S. Food and Drug Administration, 2017,  
Plecanatide (Trulance™)
Synergy Pharmaceuticals

• Adverse Reactions
  – Diarrhea (5%)
  – Upper respiratory tract infection
  – Abdominal distension
  – Flatulence
  – Abdominal tenderness
  – Increased ALT and AST

U.S Food and Drug Administration, 2017,
Plecanatide (Trulance™)
Synergy Pharmaceuticals

• Administration
  – Patients with swallowing difficulties
    Oral Administration in Applesauce:
      1. Crush the TRULANCE tablet to a powder and mix with 1 teaspoonful of room temperature applesauce
      2. Consume the entire tablet-applesauce mixture immediately
    Oral Administration in Water:
      1. Place the TRULANCE tablet in a clean cup
      2. Pour approximately 30 mL of room temperature water into the cup
      3. Mix by gently swirling the tablet and water mixture for at least 10 seconds. The TRULANCE tablet will fall apart in the water.
      4. Swallow the entire contents of the tablet water mixture immediately
      5. If any portion of the tablet is left in the cup, add another 30 mL of water to the cup, swirl for at least 10 seconds, and swallow immediately
      6. Do not store the tablet-water mixture for later use

U.S Food and Drug Administration, 2017,
Crisaborole topical (Eucrisa™)
Anacor Pharms Inc.

- **Indication:**
  - Indicated for mild-to-moderate atopic dermatitis

- **Mechanism of action:**
  - Phosphodiesterase (PDE)-4 inhibitor
    - Increased intracellular cyclic adenosine monophosphate (cAMP) levels → decrease inflammation

- **Dosing:**
  - Apply a thin layer topically to affected area(s) BID

- **Topical ointment**
  - 2%

U.S Food and Drug Administration, 2016,
Crisaborole topical (Eucrisa™)
Anacor Pharms Inc.

• Precautions
  – Hypersensitivity reactions
    • Urticaria
    • Pruritus
    • Swelling
    • Erythema

U.S Food and Drug Administration, 2016,
• Adverse Reactions
  – Application site pain, burning, or stinging (4%)
Brodalumab (Siliq™)
Valeant Pharmaceuticals

• Indication:
  – moderate-to-severe plaque psoriasis in adults

• Mechanism of action:
  – Human monoclonal IgG2 antibody that selectively binds to human IL-17R
    • Blocking IL17RA inhibits IL-17 cytokine-induced responses, including the release of proinflammatory cytokines

• Dosing:
  – 210 mg SC at Weeks 0, 1, and 2, THEN
  – 210 mg SC q2wk
  – If an adequate response has not been achieved after 12-16 weeks, consider discontinuing therapy

• **Contraindications**
  – Crohn disease

• **Precautions**
  – Increase risk of infections
  – Avoid live vaccines
  – Evaluate patients for TB before initiating
    • do not administer to patients with active TB

• **Black Box Warnings**
  – Suicidal ideation
Brodalumab (Siliq™)
Valeant Pharmaceuticals

- **Adverse Reactions**
  - Headache (3.5%)
  - Arthralgia (3.3%)
  - Fungal infections (2.4%)
  - Injection site reaction (1.3%)

U.S. Food and Drug Administration, 2017,
• **Indication:**
  - Add-on therapy for patients with Parkinson disease
    - Currently taking levodopa/carbidopa, experiencing “off” episodes

• **Mechanism of action:**
  - Unknown
    - Theory:
      - Inhibits MAO-B activity by blocking dopamine breakdown → leading to increased dopamine

• **Dosing:**
  - Initial: 50 mg PO qDay
    - After 2 weeks, may increase dose to 100 mg PO qDay, based on individual need and tolerability
    - Doses >100 mg/day have not shown additional benefit
Contraindications

- Severe hepatic impairment
- Coadministration with:
  - MAOIs
  - Potent inhibitors of MAO (linezolid)
  - SSRIs
  - Meperidine
  - Tramadol
  - TCAs
  - Cyclobenzaprine
  - Methylphenidate
  - St. John’s wort
Precautions

- Hypertension (exacerbation or new onset)
- Hallucinations
- Psychosis
- Compulsive behaviors
Safinamide (Xadago™)
Newron Pharmaceuticals

- Adverse Reactions
  - Dyskinesia (17-21%)
  - Hypertension (5-7%)
  - ALT or AST increased to >ULN (5-7%)
  - Fall (4-6%)
  - Orthostatic hypotension (2%)

- Postmarketing Reports
  - Swelling of tongue and gingiva
  - Dyspnea
  - Rash
Naldemedidine (Symproic™)
Shionogi

• Indication:
  – Treatment of opioid-induced constipation in adults with chronic noncancer pain

• Mechanism of action:
  – Opioid antagonist with binding affinities for mu-, delta-, and kappa-opioid receptors
    • peripherally acting mu-opioid receptor antagonist in the GI tract, decreasing the constipating effects of opioids

• Dosing:
  – Schedule II
  – 0.2 mg PO qDay

U.S. Food and Drug Administration, 2017,
https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/208854s000lbl.pdf
• Contraindications
  – Known or suspected GI obstruction
• Precautions
  – Gastrointestinal perforation
  – Crohn disease
  – Opioid withdrawal
• Administration
  – Discontinue naldemedine if treatment with opioids is also discontinued

Naldemedine (Symproic™)
Shionogi

U.S Food and Drug Administration, 2017,
https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/208854s000lbl.pdf
Adverse Reactions
- Abdominal pain (8-11%)
- Diarrhea (7%)
- Nausea (4-6%)
- Vomiting (3%)

Drug interaction overview
- Strong CYP3A4 inducers → decreased efficacy of naldemedine
- Moderate or strong CYP3A4 inhibitors → increased naldemedine concentrations
- P-gp inhibitors → increased naldemedine concentrations
- Avoid use with another opioid antagonist
• Indication:
  – Moderate to severe atopic dermatitis in adults whose disease is not adequately controlled with topical prescription therapies

• Mechanism of action:
  – Monoclonal antibody that inhibits IL-4 and IL-13 signaling
    • Blocking the release of proinflammatory cytokines, chemokines, and IgE

• Dosing:
  – 600 mg (ie, two 300-mg injections) SC once, then
  – 300 mg SC every other week

  – Can be used with or without topical corticosteroids
• Administration
  – SC Preparation
    • Remove syringe from the refrigerator
    • Set out at room temperature (45 min)
  – SC Administration
    • Self-administer into the thigh or abdomen
    • May inject in the upper arm if administered by a caregiver
    • Rotate injection site

• Missed dose
  – ≤7 days:
    • Administer the injection within 7 days from the missed dose and then resume the original schedule
  – >7 days:
    • Instruct patient to wait until the next scheduled dose
Dupilumab (Dupixent™)
Regeneron Pharmaceuticals

• Precautions
  – Hypersensitivity reactions
  – Conjunctivitis
  – Keratitis

• Drug interaction overview
  – Avoid coadministration with live vaccines

U.S Food and Drug Administration, 2017,
https://www.regeneron.com/sites/default/files/Dupixent_FPI.pdf
Dupilumab (Dupixent™)
Regeneron Pharmaceuticals

- Adverse Reactions
  - Injection site reactions (10%)
  - Conjunctivitis (9-10%)
  - Oral herpes (3-4%)
  - Immunogenicity, neutralizing (2%)
  - Keratitis (<1-4%)
  - Eye pruritus (1-2%)
  - Dry eye (<1-2%)
Valbenazine (Ingrezza™)
Neurocrine Biosciences

• **Indication:**
  - Treatment of adults with tardive dyskinesia

• **Mechanism of action:**
  - Unknown
    • **Theory:**
      - Reversible inhibition of vesicular monoamine transporter 2, a transporter that regulates monoamine uptake

• **Dosing:**
  - 40 mg PO qDay x1 week, then
  - Increase to 80 mg PO qDay
  - Hepatic impairment
    • Moderate-to-severe (Child-Pugh 7-15)
      - Not to exceed 40 mg/day
  - Renal impairment
    • Severe (CrCl <30 mL/min)
      - Use not recommended

Valbenazine (Ingrezza™)
Neurocrine Biosciences

• Precautions
  – Warn patients not to perform activities requiring mental alertness d/t somnolence
  – QT prolongation
    • Not clinically significant at recommending dosing
    • Coadministration with strong CYP2D6 or 3A4 inhibitors may lead to clinically significant QT prolongation
Drug Interactions

- Strong CYP3A4 inducers
  - Coadministration not recommended
- Strong CYP3A4 inhibitors
  - Reduce valbenazine dose to 40 mg/day
- Strong CYP2D6 inhibitors
  - Reduce valbenazine dose to 40 mg/day
Valbenazine (Ingrezza™)
Neurocrine Biosciences

• Adverse Reactions
  – Somnolence (10.9%)
  – Anticholinergic effects (5.4%)
  – Balance disorders/fall (4.1%)
  – Headache (3.4%)
  – Akathisia (2.7%)
  – Vomiting (2.6%)
Abaloparatide (Tymlos™)
Radius Health

• Indication:
  – Treatment of postmenopausal women with osteoporosis at high risk for fracture

• Mechanism of action:
  – Synthetic peptide analog of human parathyroid hormone-related protein
    • Naturally occurring hormone that regulates bone formation
    • increases in bone mineral density → increases in bone strength

• Dosing:
  – 80 mcg SC qDay

U.S Food and Drug Administration, 2017,
Abaloparatide (Tymlos™)
Radius Health

• Boxed warning:
  – Abaloparatide caused a dose-dependent increase in the incidence of osteosarcoma rats
  – It is unknown if abaloparatide causes osteosarcoma in humans
  – Not recommended in patients at increased risk of osteosarcoma
    • Paget disease of bone
    • unexplained elevations of alkaline phosphatase
    • bone metastases or skeletal malignancies
  – Cumulative use of abaloparatide and parathyroid hormone (PTH) analogs for >2 years not recommended

• Contraindications:
  – None
Abaloparatide (Tymlos™)  
Radius Health

• Precautions:  
  – Orthostatic hypotension

• Adverse Reactions:  
  – Injection site redness (58%)
  – Hypercalciuria (11%)
  – Dizziness (10%)
  – Injection site edema (10%)
  – Nausea (8%)
  – Orthostatic hypotension (4%)
  – Hypercalcemia (2%)

U.S Food and Drug Administration, 2017,  
Abaloparatide (Tymlos™)
Radius Health

• Administration:
  – SC injection into the abdomen
  – Rotate injection sites each day
  – Administer where the patient can sit or lie down
    • Prevent orthostatic hypotension

• Storage:
  – Before first use: refrigerate
  – After first use: Store for up to 30 days at room temperature
  – Do not freeze or subject to heat

New Dosage Forms

• Adzenys XR ODT™ (amphetamine)
  – New orally disintegrating extended release formulation for ADHD
• Onzeta™ Xsail™ (sumatriptan)
  – New nasal powder inhalation for acute migraine treatment
• Zembrace™ SymTouch™ (sumatriptan)
  – New injectable formations for acute migraine treatment
• Xtampza™ ER (oxycodone)
  – New opioid formulation for chronic, severe pain
  – Abuse-deterrent capsule
• ProAir® RespiClick (albuterol inhalation)
  – Indications for bronchospasm and exercise-induced asthma expanded to include children as young as 4 yr

U.S Food and Drug Administration, 2017,
New Dosage Forms

• Cambia® (diclofenac)
  – Powder for oral solution, quick onset for acute migraine treatment
• QuilliChew™ ER (methylphenidate)
  – Chewable extended-release tablet for ADHD
• Narcan® (naloxone)
  – New nasal spray formulation for emergency treatment of opioid overdose
• Invega Trinza™ (palperidone)
  – New longer-acting (3 months) injectable atypical antipsychotic
• Seebri™ Neohaler® (glycopyrrolate)
  – LAAC oral inhaler for COPD
• Lazanda® (fentanyl intranasal)
  – 300mcg/mL nasal spray, indicated for cancer pain

U.S. Food and Drug Administration, 2017,
New Dosage Forms

• Arymo ER® (morphine)
  – Extended-release tablets for severe pain
• Noctiva™ (desmopressin)
  – New nasal spray formulation for nocturia due to nocturnal polyuria
• Vantrela ER® (hydrocodone)
  – Extended release tablets for severe pain
## New Combinations

<table>
<thead>
<tr>
<th>Combination</th>
<th>Description</th>
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</thead>
</table>
| Bevespi Aerosphere™ | Glycopyrrolate/formoterol  
  - LAAC/LABA for COPD |
| Glyxambi® | Empagliflozin/linagliptin  
  - SGLT2 inhibitor and DPP-4 inhibitor for T2DM |
| Prestalia® | Perindopril/amlodipine  
  - ACEi + CCB for hypertension |
| Utibron™ Neohaler® | Indacaterol/glycopyrrolate  
  - LABA + LAAC inhaler for COPD |
| Stiolto® Respimat® | Tiotropium/olodaterol  
  - LAAC + LABA for COPD |
| Synjardy® | Empagliflozin/metformin  
  - SGLT2 inhibitor and metformin for T2DM |
| Ryzodeg® | Insulin degludec/insulin aspart  
  - 70/30 mix insulin for DM |
| Byvalson | Nebivolol/valsartan  
  - Beta blocker/ARB for hypertension |

U.S Food and Drug Administration, 2017,
New Combinations

- **Airduo Respiclick™**
  - Fluticasone/salmeterol
    - ICS/LABA for asthma

- **Armonair Respiclick®**
  - Fluticasone
    - ICS for asthma

- **Qtern®**
  - Dapagliflozin/saxagliptin
    - SGLT2 inhibitor and DPP-4 inhibitor for T2DM

U.S Food and Drug Administration, 2017,
Generic Drugs in 2015 - 2017

- Avodart®
  - Dutasteride
- Crestor®
  - Rosuvastatin
- Exelon®
  - Rivastigmine TD
- Frova®
  - Frovatriptan
- Nasonex®
  - Mometasone nasal spray
- OxyContin®
  - Oxycodone ER
- Ritalin LA®
  - Methylphenidate ER
- Voltaren®
  - Diclofenac 1% gel

U.S Food and Drug Administration, 2017,
## Generic Drugs in 2015 - 2017

<table>
<thead>
<tr>
<th>Brand</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Azor®</td>
<td>Olmesartan/amlodipine</td>
</tr>
<tr>
<td>Benicar®/Benicar HCT®</td>
<td>Olmesartan +/- HCTZ</td>
</tr>
<tr>
<td>Aggrenox®</td>
<td>Aspirin/dipyridamole</td>
</tr>
<tr>
<td>Lantus®</td>
<td>Insulin glargine</td>
</tr>
<tr>
<td>Seroquel XR®</td>
<td>Quetiapine ER</td>
</tr>
<tr>
<td>Zegerid®</td>
<td>Omeprazole/Na bicarbonate</td>
</tr>
<tr>
<td>Invega®</td>
<td>Paliperidone ER</td>
</tr>
<tr>
<td>Lescol XL®</td>
<td>Fluvastatin ER</td>
</tr>
<tr>
<td>Tamiflu®</td>
<td>Oseltamivir</td>
</tr>
<tr>
<td>Zyvox®</td>
<td>Linezolid oral suspension</td>
</tr>
</tbody>
</table>

U.S. Food and Drug Administration, 2017,
Upcoming Generic Drugs in 2017 – 2018

- **ProAir® HFA**
  - Albuterol

- **Strattera™**
  - Atomoxetine
    - available

- **Relpax®**
  - Eletriptan

- **Vytorin® (2017)**
  - Ezetimibe/simvastatin
    - available

- **Zetia® (2017)**
  - Ezetimibe
    - available

- **Viagra® (2017)**
  - Sildenafil

U.S Food and Drug Administration, 2017,
Drug Changes

• Trintellix (vortioxetine) – brand named changed from Brintellix
  – Due to sound-a-like & look-a-like issues with Brillinta (ticagrelor)
• Prevnar 13 (pneumococcal vaccine 13-valent) – FDA approved for use in adults 18 – 49 yr with immunocompromised conditions

U.S Food and Drug Administration, 2017,
Drugs Withdrawn from Market – 2015 - 2017

- **Elepsia XR**
  - Levetiracetam extended release
    - FDA revoked approval
    - Manufacturing quality problems

- **Advicor**
  - Niacin ER/lovastatin
    - FDA revoked approval
    - Safety and efficacy concerns

- **Simcor**
  - Niacin ER/simvastatin
    - FDA revoked approval
    - Safety and efficacy concerns

- **Niaspan**
  - Niacin
    - FDA revoked approval
    - Manufacturing quality problems

- **Trilipix**
  - Fenofibric acid
    - FDA revoked approval
    - Safety and efficacy concerns

- **Opana ER**
  - Oxymorphone
    - Benefit no longer outweigh risk

U.S Food and Drug Administration, 2017,
Removal of FDA Indication

• FDA Statement on coadministration of a statin with niacin and/or fibrate products:
  – Scientific evidence no longer supports drug induced TG lowering and/or increasing HDL in statin-treated patients to reduce the risk of cardiovascular events
    • Niacin ER (Niaspan)
    • Fenofibric acid (Trilipix)
    • Lovastatin–niacin ER (Advicor)
    • Simvastatin-niacin ER (Simcor)

How many new molecular entities were approved in 2016?

a) 22  
b) 27  
c) 41  
d) 45
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Post-Test Questions

What medical indication was ixekizumab approved for?

a) Plaque psoriasis
b) Type 2 Diabetes
c) Hyperlipidemia
d) Hepatitis C
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Post-Test Questions

What medical indication was valbenazine approved for?

a) Osteoporosis  
b) Bipolar disorder  
c) Tardive dyskinesia  
d) Opioid-induced constipation
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What medical indication was valbenazine approved for?

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What medical indication was plecanatide approved for?

a) Dermatitis  
b) Constipation  
c) Type 2 Diabetes  
d) Multiple sclerosis
What medical indication was plecanatide approved for?

a) Dermatitis

b) **Constipation**

c) Type 2 Diabetes

d) Multiple sclerosis
Take Home Points

• There have already been more NME approvals in 2017 than in 2016
• New medications are constantly being reviewed and approved by the FDA
• This changes the treatment options for patients and prescribers
• As pharmacist and pharmacy technicians we must be vigilant to keep up with these new medications and at the very least know where to quickly find information related to new medications
Resources & References

FDA New Drug Innovation webpage:

CenterWatch webpage for newly approved medications
• http://www.centerwatch.com/drug-information/fda-approved-drugs/

Pharmacist Letter webpage for newly approved medications
Resources & References

• Package Inserts:
  – http://www.xadago.com/XADAGO_FullPI.pdf
  – https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/208854s000lbl.pdf
  – http://ingrezza.com/HCP/PI