New Drugs and Drug News of 2018

Pharmacy practitioners need to be knowledgeable about new drugs introduced to the market, and public health advisories about drug therapy.

Learning Objectives

**Pharmacist**
1. Recognize the approved indication, common adverse effects and drug interactions for new drugs approved by the FDA in 2018.
2. For each new medication approved in 2018, identify the burden-to-benefit ratio of therapy.
3. Identify important drug alerts by the FDA (Public Health Advisories) and implications for patient care.

**Pharmacy Technician**
1. Recognize the approved indication, common adverse effects and drug interactions for new drugs approved by the FDA in 2018.
2. For each new medication approved in 2018, identify the burden-to-benefit ratio of therapy.
3. Identify important drug alerts by the FDA (Public Health Advisories).

**Nurse**
1. Recognize the approved indication, common adverse effects and drug interactions for new drugs approved by the FDA in 2018.
2. For each new medication approved in 2018, identify the burden-to-benefit ratio of therapy.
3. Identify important drug alerts by the FDA (Public Health Advisories) and implications for patient care.
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Target Audience
Pharmacists, Pharmacy Technicians, Nurses

Universal Activity Number
Pharmacist
0798-0000-19-008-L01-P
Pharmacy Technician
0798-0000-19-008-L01-T
Nurse
0798-0000-19-008-L01-P

Credit Hours
1.25 Hour

Activity Type
Knowledge-Based

CE Broker Tracking Number
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Activity Offline Date
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ACPE Expiration Date
March, 2019

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PharmCon, Inc.
NEW DRUGS AND DRUG NEWS OF 2018

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LEARNING OBJECTIVES

• At the conclusion of this program, the participant will be able to:
  • Recognize the approved indication, common adverse effects and drug interactions for new drugs approved by the FDA in 2018.
  • For each new medication approved in 2018, identify the burden-to-benefit ratio of therapy.
  • Identify important drug alerts by the FDA (Public Health Advisories) and implications for patient care.
2018 NEW DRUG APPROVALS

- BANNER YEAR!
- US Regulators approved a total of SIXTY-ONE drugs
- 59 by FDA’s Center for Drug Evaluation and Research (from 51 companies)
- 2 recombinant therapies (Andexxa and Jivi) by the Center for Biologics Evaluation and Research

CDER NME NDAs/BLAs†
Filings and Approvals by CY as of 11/30/18

† Multiple applications pertaining to a single new molecular/biologic entity are only counted once. Original BLAs that do not contain a new active ingredient are excluded.

* This information is accurate as of November 30th, 2018. In rare instances, it may be necessary for FDA to change a drug’s new molecular entity (NME) designation or the status of its application as a new biologics license application (BLA). This note applies to all references to NME/Original BLA in this presentation.

Since applications are received and filed throughout a calendar year, the filed applications in a given calendar year do not necessarily correspond to an approval in the same calendar year. Certain applications are within their 30-day filing review period and may not be filed upon completion of the review.

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New Drugs and Drug News of 2018

2018 NEW DRUG APPROVALS

• 31 of the new drugs are for rare diseases
• 31 are orphan drugs
• 26 were priority reviews
• 16 were fast-track
• 12 were breakthrough therapy

DERMATOLOGY

<table>
<thead>
<tr>
<th>Generic</th>
<th>Trade</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tildrakizumab</td>
<td>Illumya</td>
<td>Treatment of plaque psoriasis</td>
</tr>
<tr>
<td>Glycopyrronium</td>
<td>Qbrexza</td>
<td>For the treatment of primary axillary hyperhidrosis</td>
</tr>
<tr>
<td>Sarecycline</td>
<td>Seysara</td>
<td>For the treatment of moderate to severe acne vulgaris in patients</td>
</tr>
</tbody>
</table>
<pre><code>             |       | 9 years of age and older                                          |
</code></pre>

Endocrine

<table>
<thead>
<tr>
<th>Generic</th>
<th>Trade</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Semaglutide</td>
<td>Ozempic</td>
<td>Glucagon-like peptide</td>
</tr>
<tr>
<td>Ertugliflozin</td>
<td>Steglatro</td>
<td>Adjunct to diet/exercise for the management of type 2 diabetes</td>
</tr>
</tbody>
</table>
**GLYCOPPYRONIUM (QBREXZA)**

- Indication/MOA – anticholinergic indicated for topical treatment of primary axillary hyperhidrosis in adults and pediatric patients 9 years of age and older
- Dosage – apply once daily to both axillae using a single cloth (pre-moistened with 2.4% glycopyrronium solution)
- Contraindications – patients with medical conditions that can be exacerbated by anticholinergic effects (glaucoma, paralytic ileus, unstable CV state in acute hemorrhage, severe ulcerative colitis, toxic megacolon, myasthenia gravis, Sjogren’s syndrome)

**AE** – dry mouth, mydriasis, oropharyngeal pain, headache, urinary hesitation, vision blurred, nasal dryness, dry throat, dry eye, dry skin, constipation.
- Local skin reactions, including erythema, burning/stinging and pruritus are also common.
- Drug interaction – coadministration with anticholinergic medications
GLYCOPRORRONIUM (QBREXZA)

• Clinical trial inclusion criteria – all subjects produced at least 50 mg of sweat in each axilla (gravimetrically measured) over a 5-minute period and rated the severity of their sweating daily over a week as ≥ 4 (0-10 scale)

<table>
<thead>
<tr>
<th></th>
<th>Trial 1</th>
<th>Vehicle</th>
<th>Trial 2</th>
<th>Vehicle</th>
</tr>
</thead>
<tbody>
<tr>
<td>Response at Week 4 (% with ≥ 4 point improvement from baseline)</td>
<td>53%</td>
<td>28%</td>
<td>66%</td>
<td>27%</td>
</tr>
<tr>
<td>Change from baseline in sweat production at week 4 (mg/5 minutes)</td>
<td>-81</td>
<td>-66</td>
<td>-79</td>
<td>-58</td>
</tr>
</tbody>
</table>

Each cloth $22  Botox ~ $2400 q6months; Qbrexza ~ $4,000 q6months

SEMAGLUTIDE (OZEMPIC)

• The 6th glucagon-like peptide-1 (GLP-1) approved
  • Exenatide (Byetta, Bydureon), liraglutide (Victoza), lixisenatide (Adlyxin), dulaglutide (Trulicity)

• Indication – Given SQ qweek as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus

• MOA – suppression of glucagon secretion, stimulation of glucose-dependent insulin secretion, slowing gastric emptying, and promoting satiety (4-5 kg weight loss; ~1.5% reduction in A1c)

• Warnings – thyroid C-cell tumors (rodents), medullary thyroid carcinoma, endocrine neoplasia syndrome type 2, pancreatitis

• AE – nausea (20%), vomiting (9%), diarrhea (9%), abd pain (6%)

$600 per weekly dose
ERTUGLIFLOZIN L-PYROGLUTAMIC ACID (STEGLATRO)

• Sodium-glucose cotransporter 2 (SGLT2) inhibitor
  • Canagliflozin (Invokana), dapagliflozin (Farxiga), empagliflozin (Jardiance; ↓ risk CV disease)
• Indicated as adjunct to diet/exercise in type 2 diabetes
• Advantages – risk of lower limb amputation not as definitive as canagliflozin; not associated with bladder cancer (vs. dapagliflozin)
• AE – female genital mycotic infection (12%), male genital mycotic infection (4%), UTI (4%), headache (3%), back pain (3%), ↑ LDL (5%)
• Dose – initially 5 mg po qd; may be increased to 15 mg po qd
• Do not initiate therapy with eGFR of 30-60 ml/min

$11 per tablet

FDA DRUG SAFETY COMMUNICATION
ALERT
SGLT-2 INHIBITORS (CANAGLIFLOZIN, DAgGLIFLOZIN, EMPAGLIFLOZIN, ERTUGLIFLOZIN)

• Rare but serious infection of the genitals and area around genitals have been reported
• AKA necrotizing fasciitis of perineum; Fournier’s gangrene
• Advise patients to seek medication attention with complaints of tenderness, redness, or swelling of the genitals or the area from the genitals back to the rectum, and have a fever above 100.4°F or a general feeling of being unwell.
• Symptoms worsen quickly
• Tx – broad spectrum antibiotics and surgical debridement prn

SGLT2 inhibitors have also been associated with euglycemic DKA

Gastroenterology

<table>
<thead>
<tr>
<th>Generic</th>
<th>Trade</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prucalopride</td>
<td>Motegrity</td>
<td>For the treatment of chronic idiopathic constipation</td>
</tr>
</tbody>
</table>
**IMODIUM (LOPERAMIDE) FOR OTC USE**

- FDA requiring manufacturers to use blister packs or other single dose packaging and to limit the number of doses in a package.
- FDA continues to receive reports of serious heart problems and deaths with much higher than the recommended doses of loperamide, primarily among people who are intentionally misusing or abusing the product, despite added warnings.
- Maximum daily dose is 8 mg/day OTC, 16 mg/day Rx.

**GENETIC DISEASE**

<table>
<thead>
<tr>
<th>Generic</th>
<th>Trade</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Buroseumab</td>
<td>Crysvita</td>
<td>For the treatment of X-linked hypophosphatemia</td>
</tr>
<tr>
<td>Migalastat</td>
<td>Galafold</td>
<td>For the treatment of Fabry Disease</td>
</tr>
<tr>
<td>Patisiran</td>
<td>Onpattro</td>
<td>For the treatment of the polyneuropathy of hereditary transthyretin-mediated amyloidosis in adults</td>
</tr>
<tr>
<td>Inotersen</td>
<td>Tegsedi</td>
<td>For the treatment of adenosine deaminase severe combined immune deficiency</td>
</tr>
<tr>
<td>Elapegademase</td>
<td>Revcovi</td>
<td>For the treatment of adenosine deaminase severe combined immune deficiency</td>
</tr>
</tbody>
</table>

**Immunology**

<table>
<thead>
<tr>
<th>Generic</th>
<th>Trade</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Emapaglumab</td>
<td>Gamifant</td>
<td>For the treatment of primary hemophagocytic lymphohistiocytosis</td>
</tr>
<tr>
<td>Lanadelumab</td>
<td>Takhzyro</td>
<td>For the prevention of hereditary angioedema attacks</td>
</tr>
</tbody>
</table>
### HEMATOLOGY

**Generic** | **Trade** | **Indication**
--- | --- | ---
Coagulation factor X1 (recombinant, inactivated) | Andexxa | For the reversal of factor Xa inhibitors
Avtrombopag | Doptelet | For the treatment of thrombocytopenia in adults with chronic liver disease scheduled to undergo a procedure
Lusutrombopag | Mulpleta | For the treatment of thrombocytopenia in adults with chronic liver disease scheduled to undergo a procedure
Sodium zirconium cyclosilicate | Lokelma | For the treatment of hyperkalemia
Pegvaliase | Palynziq | For the treatment of phenylketonuria
Mogamulizumab | Poteligeo | For the treatment of mycosis fungoides of Sézary syndrome
Fostamatinib disodium hexahydrate | Tavalisse | For the treatment of chronic immune thrombocytopenia

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**Generic** | **Trade** | **Indication**
--- | --- | ---
Ravulizumab | Ultomiris | For the treatment of paroxysmal nocturnal hemoglobinuria
Gilteritinib | Xospata | For the treatment of acute myeloid leukemia with a FLT3 mutation
Antithemophilic factors (recombinant) | Jivi | For hemophilia A
COAGULATION FACTOR XA INACTIVATED (ANDEXXA)

• Accelerated approval by FDA for urgent reversal of the anticoagulant effect of the direct factor Xa inhibitors:
  • Apixaban (Eliquis) and rivaroxaban (Xarelto)
    • Has NOT been approved for reversal of anticoagulation with edoxaban (Savaysa) or betrixaban (Bveyxxa)
    • Has NOT been approved for reversal of indirect factor Xa inhibitors enoxaparin and fondaparinux (although it is expected to be efficacy with all these agents)
  • Idarucizumab (Praxbind) was approved in 2015 for reversal of the anticoagulant effect of the direct thrombin inhibitor dabigatran (Pradaxa)

MOA – Andexanet alfa is a genetically modified variant of human factor Xa (alanine is substituted for serine) produced in the Chinese hamster ovary cell line
  • Acts as a decoy, binding to factor Xa inhibitors and neutralizing their anticoagulant effect

AE – labeling includes boxed warning about risk of thromboembolic, ischemic, and cardiac events, including sudden death
  • 11% of patients had a thrombotic event and 12% died within 30 days after administration of the drug
COAGULATION FACTOR XA INACTIVATED (ANDEXXA)

• Efficacy – two studies, evaluating mean change from baseline in anti-factor Xa activity
  • 66 healthy subjects received apixaban 5 mg twice daily for 3.5 days
  • Three hours after last dose, subjects received andexanet alfa (400 mg IV bolus with or without subsequent 4 mg/minute continuous infusion for 2 hours) or placebo
  • Anti-factor Xa activity was reduced within 2-5 minutes by 94% with andexanet alfa IV bolus, vs. 21% with placebo
  • Thrombin generation was fully restored within 2-5 minutes in 100% of andexanet-treated patients vs. 11% placebo-treated patients
  • Similar results with a rivaroxaban study (800 mg IV andexanet alfa)

COAGULATION FACTOR XA INACTIVATED (ANDEXXA)

• Dosing
  • Patients taking < 10 mg rivaroxaban or < 5 mg apixaban per dose should receive low-dose regimen – 400 mg IV bolus dose of andexanet alfa, followed by a 4 mg/minute continuous infusion for up to 120 minutes
  • Patients taking > 10 mg of rivaroxaban or > 5 mg apixaban per dose should receive the high-dose regimen – 800 mg IV bolus dose of andexanet alfa, followed by an 9 mg/minute continuous infusion for up to 120 minutes if their last dose was < 8 before starting andexanet alfa; if the last dose was > 8 hours before starting andexanet alfa, the low-dose regimen should be used. If unknown, use the high-dose regimen

Cost of high dose regimen is approximately $50,000
### INFECTIOUS AND INFECTIOUS DISEASES

<table>
<thead>
<tr>
<th>Generic</th>
<th>Trade</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bictegravir/emtricitabine/tenofovir alafenamide</td>
<td>Biktarvy</td>
<td>For the treatment of HIV-1 infection in adults</td>
</tr>
<tr>
<td>Doravirine, lamivudine, and tenofovir disoproxil fumarate</td>
<td>Delstrigo</td>
<td>For the treatment of HIV-1 infection</td>
</tr>
<tr>
<td>Doravirine</td>
<td>Pifeltro</td>
<td>For the treatment of HIV-1 infection</td>
</tr>
<tr>
<td>Darunavir, cobicistat, emtricitabine, and tenofovir alafenamide</td>
<td>Symtuza</td>
<td>For the treatment of HIV-1 infection</td>
</tr>
<tr>
<td>Ibalizumab</td>
<td>Trogarzo</td>
<td>For the treatment of multidrug resistant HIV-1 infection</td>
</tr>
<tr>
<td>Tafenoquine</td>
<td>Krintafel</td>
<td>For the prevention of malaria relapse in patients receiving appropriate antimalarial therapy</td>
</tr>
<tr>
<td>Rifamycin</td>
<td>Aemcolo</td>
<td>For the treatment of traveler's diarrhea</td>
</tr>
<tr>
<td>Eravacycline</td>
<td>Xerava</td>
<td>For the treatment complicated intra-abdominal infections</td>
</tr>
</tbody>
</table>

### INFECTIOUS AND INFECTIOUS DISEASES

<table>
<thead>
<tr>
<th>Generic</th>
<th>Trade</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diphtheria, tetanus, pertussis, poliomyelitis, hepatitis B, Haemophilus influenzae type b</td>
<td>Vaxelis</td>
<td>For the prevention of diphtheria, tetanus, pertussis, poliomyelitis, hepatitis B, and Haemophilus influenzae type b</td>
</tr>
<tr>
<td>Moxidectin</td>
<td></td>
<td>For the treatment of onchocerciasis (river blindness)</td>
</tr>
<tr>
<td>Omadacycline</td>
<td>Nuzyra</td>
<td>For the treatment of community-acquired bacterial pneumonia and acute bacterial skin and skin structure infections</td>
</tr>
<tr>
<td>Baloxavir marboxil</td>
<td>Xofluza</td>
<td>For the treatment of acute uncomplicated influenza</td>
</tr>
<tr>
<td>Plazomicin</td>
<td>Zemdri</td>
<td>For the treatment of complicated urinary tract infections</td>
</tr>
<tr>
<td>Delafloxacin meglumine</td>
<td>Baxdela</td>
<td>For the treatment of adults with acute bacterial skin and skin structure infections (IV or oral)</td>
</tr>
</tbody>
</table>
NEW DRUGS AND DRUG NEWS OF 2018

INFECTIONOUS AND INFECTIOUS DISEASES

<table>
<thead>
<tr>
<th>Generic</th>
<th>Trade</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tecovirimat</td>
<td>Tpoxx</td>
<td>For the treatment of smallpox</td>
</tr>
<tr>
<td>Obiltoxaximab</td>
<td>Anthim</td>
<td>Treatment of inhalational anthrax in combination with antibacterial drugs and prophylaxis of inhalational anthrax when other therapies are unavailable or inappropriate.</td>
</tr>
</tbody>
</table>

DELAFLOXACIN MEGLUMINE (BAXDELA)

- Fluoroquinolone antibacterial with broad spectrum of action (PO/IV)
- Indication – Tx of adults with acute bacterial skin and skin structure infections
  - *S. aureus* (including MRSA), other *Staph, Strep, Enterococcus, Escherichia, Enterobacter, Klebsiella, Pseudomonas*
- First FQ shown to be effective in tx of infections caused by MRSA
  - Non-inferior to vancomycin + aztreonam combination
  - 80% of patients had ≥ 20% decrease in lesion size at 48-72 hours
  - > 95% treatment success at 14 days
  - It’s effectiveness as a single agent that can be given orally provides an advantages over the concurrent use of IV vancomycin + aztreonam
DELAFLOXACIN MEGLUMINE (BAXDELA)

• Dose
  • 450 mg po ~ 300 mg IV
  • 300 mg IV every 12 hours over 60 minutes
  • 450 mg po every 12 hours
  • May be initiated IV and switched to oral
  • Treatment duration 5-14 days
  • IV – reduce by 50% for severe renal impairment
• AE – nausea (8%), diarrhea (8%), headache (3%), transaminase elevations (3%)

$81/dose

MORE FQ WARNINGS

• FDA has required changes in the labeling of all systemic FQ antibiotics – severe hypoglycemia and mental health effects
• Most hypoglycemia cases were in patients with diabetes, older age, renal insufficiency
• Labeling must include warnings of delirium, agitation, nervousness, and disturbances in attention, memory and orientation.
  • Can occur after a single FQ dose; DC therapy
• Systemic FQ therapy may also cause permanent peripheral neuropathy, tendinitis, tendon rupture, exacerbation of myasthenia gravis, *Clostridium difficile* infection, QT-prolongation (except delafloxacin).

Avoid FQ use in uncomplicated UTI, acute sinusitis, acute exacerbation of chronic bronchitis, unless no alternate treatment option is available.
**BALOXAVIR MARBOXIL (XOFLUZA)**

- Baloxavir marboxil is a prodrug that is almost completely converted by hydrolysis to its active metabolite, baloxavir
  - Activity against influenza A and influenza B viruses
- Indication – treatment of acute uncomplicated influenza in patients ≥ 12 yo who have been symptomatic for no more than 48 hours
- Dosing
  - Patients weighing 40 kg to < 80 kg – single dose of 40 mg
  - Patients weighing at least 80 kg – single dose of 80 mg
- AE – diarrhea (3%), bronchitis (2%)

**Advantages**
- Single dose treatment (oseltamivir bid for 5 days)
- Unique MOA (polymerase acidic endonuclease inhibitor)
- May be effective in patients with influenza resistant to oseltamivir
- Use not associated with neuropsychiatric adverse effects
- No dosage adjustment in renal impairment required

**Disadvantages**
- Effectiveness/safety not established < 12 yo (oseltamivir indicated ≥ 2 weeks old)
- May be less effective against influenza B
- Has not been evaluated for the prophylaxis of influenza (oseltamivir has indication)
- Absorption and activity may be reduced by coadministration with polyvalent cation-containing products (antacids)
- May decrease the effectiveness of intranasal live attenuated influenza vaccine
- $155 for baloxavir vs. $45 with oseltamivir

Median time to alleviation of symptoms ~ 50 hours vs. 80 hours with placebo
BIOTERRORISM - ANTHIM

- Anthim - obiltotoxaximab
- Inhalational anthrax – caused by inhalation of the spores of *Bacillus anthracis* is a continuing concern because of its potential use as a bioterrorism agent
  - Death is caused by a toxin, so treatment must include both antimicrobials and antitoxins
  - Raxibacumab was previously approved
  - Both are manufactured only for the CDC national stockpile
- AE – hypersensitivity reactions (10.6%), anaphylaxis (0.9%)
- IV infusion over 90 minutes

TECOVIRIMAT (TPOXX)

- Indication – Treatment of human smallpox disease caused by variola virus in adult and pediatric patients weighing at least 13 kg
- Limitations of Use – Effectiveness has not been determined in humans because adequate and well-controlled field trials have not been feasible. Inducing smallpox in humans to study the drug’s effects is not ethical.
- Dose ≥ 40 kg – 600 mg twice daily x 14 days (take 30 minutes after a full meal of moderate or high fat (increases absorption 39%)
- Dose 13-40 kg – weight based for 14 days

May be mixed in liquid or soft food. Consume within 30 minutes of preparation.
TECOVIRIMAT (TPOXX)

- AE – headache (12%), nausea (5%), abdominal pain (2%), vomiting (2%)
- Drug interactions
  - Repaglinide serum level increased (hypoglycemic risk)
  - Midazolam serum level decreased (reduced effectiveness)
- Clinical trials done in animal models
NEW DOSAGE FORM - FIRVANQ

- Vancomycin hydrochloride powder for oral solution, equivalent to 3.75 g, 7.5 g, 10.5 g, 15 g vancomycin and grape-flavored diluent

<table>
<thead>
<tr>
<th>Vancomycin Concentration after Reconstitution</th>
<th>Final Volume of FIRVANQ™ after Reconstitution</th>
<th>Vancomycin Strength per Bottle</th>
<th>Diluent for FIRVANQ™</th>
</tr>
</thead>
<tbody>
<tr>
<td>25 mg/mL</td>
<td>150 mL</td>
<td>3.75 g</td>
<td>147 mL</td>
</tr>
<tr>
<td></td>
<td>300 mL</td>
<td>7.5 g</td>
<td>295 mL</td>
</tr>
<tr>
<td>50 mg/mL</td>
<td>150 mL</td>
<td>7.5 g</td>
<td>145 mL</td>
</tr>
<tr>
<td></td>
<td>210 mL</td>
<td>10.5 g</td>
<td>203 mL</td>
</tr>
<tr>
<td></td>
<td>300 mL</td>
<td>15 g</td>
<td>289 mL</td>
</tr>
</tbody>
</table>

NEW DOSAGE FORM - ZTLIDO

- ZTLido contains lidocaine, an amide local anesthetic, indicated for relief of pain associated with post-herpetic neuralgia
- ZTLido is 1.8% but has enhanced bioavailability, and is equivalent to Lidoderm 5%
- Can apply up to three patches; patches may be cut; 12 hours on/12 hours off

<table>
<thead>
<tr>
<th></th>
<th>ZTLido</th>
<th>Lidoderm</th>
</tr>
</thead>
<tbody>
<tr>
<td>30 patches</td>
<td>$285.00</td>
<td>$75.00</td>
</tr>
</tbody>
</table>
## MUSCULOSKELETAL

**Generic** | **Trade** | **Indication**
--- | --- | ---
Amifampridine | Firdapse | For the treatment of Lambert-Eaton myasthenic syndrome

## Nephrology

**Generic** | **Trade** | **Indication**
--- | --- | ---
Tolvaptan | Jynarque | For the treatment of autosomal dominant polycystic kidney disease

## NEUROLOGY

**Generic** | **Trade** | **Indication**
--- | --- | ---
Erenumab | Aimovig | For the preventive treatment of migraine in adults
Fremanezumab | Ajovy | For the treatment of migraine
Galcanezumab | Emgality | For the preventive treatment of migraine in adults
Stiripentol | Diacomit | For the treatment of seizures associated with Dravet syndrome
Cannabidiol | Epidiolex | For the treatment of seizures associated with Lennox-Gastaut syndrome or Dravet syndrome
Sufentanil | Dsuvia | For the treatment of acute pain
Amiframpridine | Firdapse | For the treatment of Lambert-Eaton myasthenic syndrome
CALCITONIN GENE-RELATED PEPTIDE-TARGETED THERAPIES FOR MIGRAINE AND CLUSTER HEADACHE

• Calcitonin gene-related peptide (CGRP) was initially identified in 1982
• It’s a 37 amino-acid signaling neuropeptide intricately involved in migraine and other headache and facial pain disorders
• CGRP has a high affinity for the CGRP receptor, located in the vasculature, trigeminal sensory afferents, the trigeminal ganglion, and the trigeminal nucleus caudalis
• Exogenous CGRP infusion triggers a migraine attack in migraine sufferers
• CGRP is a potent vasodilator of intracranial and extracranial vessels as well as centrally modulating vascular nociception

CGRP ANTAGONISTS

<table>
<thead>
<tr>
<th></th>
<th>Fremazumab (Ajovy)</th>
<th>Erenumab (Aimovig)</th>
<th>Galcanezumab (Emgality)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Indication</strong></td>
<td>Preventive treatment of migraine in adults</td>
<td>Injection site reactions (45% vs. 38% with placebo)</td>
<td></td>
</tr>
<tr>
<td><strong>Adverse effects</strong></td>
<td>Administer SQ 225 mg once a month, or 675 mg every 3 months. The 675 mg dose is administered as 3 consecutive injections of 225 mg each.</td>
<td>Administer SQ 70 mg once a month; some patients may benefit from 140 mg once a month which is administered as two consecutive injections of 70 mg each.</td>
<td>Loading dose of 240 mg SQ (2 consecutive injections of 120 mg each). Monthly dose of 120 mg. SQ in abdomen, thigh, back or upper arm, buttocks.</td>
</tr>
<tr>
<td><strong>Dosing</strong></td>
<td>Effectiveness</td>
<td>Cost</td>
<td></td>
</tr>
<tr>
<td></td>
<td>About 50% of patients treated experience a 50% reduction in headache frequency.</td>
<td>~ $600/month ($7,000/year)</td>
<td></td>
</tr>
<tr>
<td><strong>Cost</strong></td>
<td>Keep your eye on neurostimulation – a handheld device that patients use at home. Single-pulse transcranial stimulation can both prevent and treat a migraine attack.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
SO HOW DO THE CGRP ANTAGONISTS WORK?

• Ajovy
• Aimovig
• Emgality

Look for mechanism of action.

ESKETAMINE! (SPRAVATO NASAL SPRAY)

• “Watershed” moment in the treatment of depression
• First “rapid-acting” medication for depression
• NMDA-receptor antagonist
• Indicated WITH an oral antidepressant, for the treatment of treatment-resistant depression
• Must be administered under the direct supervision of a healthcare provider
• Treatment session consists of nasal administration of Spravato and post-administration observation under supervision
ESKETAMINE (SPRAVATO)

- Avoid food for at least 2 hours before administration, and avoid drinking liquids at least 30 minutes prior to administration (some experience N/V)
- Assess BP prior to dosing
  - If > 140 mmHg SBP or > 90 mmHg DBP weigh risks and benefits
  - Do not administer if increase in BP or intracranial pressure poses a serious risk
  - Reassess BP 40 minutes after administration (correlates with Cmax)
  - DC patient after two hours if BP normal

MADRS – Montgomery-Asberg Depression Rating Scale
Ten-item, clinical-rated scale, 0-60 (higher score = more severe depression)
**ESKETAMINE (SPRAVATO)**

<table>
<thead>
<tr>
<th>Induction Phase</th>
<th>Weeks 1-4</th>
<th>Adults</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Administer twice a week</td>
<td>Day 1 starting dose: 56 mg Subsequent doses: 56 or 84 mg</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Maintenance Phase</th>
<th>Weeks 5-8</th>
<th>Adults</th>
</tr>
</thead>
<tbody>
<tr>
<td>Administer once weekly</td>
<td>56 mg or 84 mg</td>
<td></td>
</tr>
<tr>
<td>Week 9 and after</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Administer every 2 weeks or once weekly</td>
<td>56 mg or 84 mg</td>
<td></td>
</tr>
</tbody>
</table>

Nasal spray device delivers a total of 28 mg (one spray/nostril). Use 2 devices for 56 mg dose; 3 devices for 84 mg dose. Allow a 5-minute rest between use of each device.

$4,720 to 6,785/month

---

**STIRIPENTOL (DIACOMIT)**

- Indication – for the treatment of seizures associated with Dravet syndrome in patients 2 years of age and older taking clobazam.
- Dosage – 50 mg/kg/day, administered by mouth in 2 or 3 divided doses
- Capsules must be swallowed whole
- Powder for suspension should be mixed in a glass of water and taken immediately after mixing during a meal.
- Warnings – somnolence, decreased appetite and decreased weight, neutropenia, thrombocytopenia, withdrawal, contains phenylalanine (PKU risk)
- Monitor for suicidal thoughts or behaviors
- AE (> 10%) – somnolence, decreased appetite, agitation, ataxia, weight decreased, hypotonia, nausea, tremor, dysarthria, insomnia
**STIRIPENTOL (DIACOMIT)**

- MOA – unknown; possibly a GABA effect, and indirect effects involving inhibition of cytochrome P450 activity with resulting increase in blood levels of clobazam and its active metabolite

<table>
<thead>
<tr>
<th></th>
<th>Study 1</th>
<th>Study 2</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Diacomit</td>
<td>Placebo</td>
</tr>
<tr>
<td># responders/total</td>
<td>71%</td>
<td>5%</td>
</tr>
<tr>
<td>(responder - &gt; 50%</td>
<td>decrease in</td>
<td>generalized</td>
</tr>
<tr>
<td>% change from baseline in seizure frequency</td>
<td>-91%</td>
<td>7.4%</td>
</tr>
</tbody>
</table>

---

**CANNABIDIOL (EPIDIOLEX)**

- Approved by FDA in June 2018 for treatment of seizures associated with:
  - Lennox-Gastaut syndrome and Dravet syndrome in patients 2 years and older.
  - Rare, severe, refractory epilepsy syndromes with onset in early childhood.
  - Both are categorized as developmental and epileptic encephalopathies, which contributes to developmental delay and behavioral abnormalities beyond the pathology of the underlying disease.
  - Characterized by multiple seizure types that are generally refractory to many of the drugs typically used for the treatment of seizures.
  - Higher rates of mortality than the general epilepsy population due to status epilepticus and sudden unexpected death.
- Prepared from *Cannabis sativa* plant (new molecular entity)
CANNABIDIOL (EPIDIOLEX)

• Clinical efficacy
  • Study 1414 – 14 week, multicenter, randomized, double-blind, placebo-controlled trial in patients with LGS
  • 225 patients randomized to CBD 10 mg/kg/day (bid); CBD 20 mg/kg/day (bid) or placebo
  • Primary endpoint – percentage change from baseline in drop seizure frequency
  • Secondary endpoints
    • # patient responders
    • % changes in total seizures/day
    • Change in S/CIG (Subjective Caregiver Global Impression of Change)

• Statistically significant differences between each CBD group vs. placebo

Table 1: Primary Endpoint Analysis Results from Study 1414 (LGS)

<table>
<thead>
<tr>
<th>Drop Seizure Frequency (per 28 Days)</th>
<th>20 mg/kg/day (N=76)</th>
<th>10 mg/kg/day (N=73)</th>
<th>Placebo (N=76)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline Period Median</td>
<td>85.5</td>
<td>86.9</td>
<td>80.3</td>
</tr>
<tr>
<td>Treatment Period Median</td>
<td>44.9</td>
<td>50.0</td>
<td>72.7</td>
</tr>
<tr>
<td>Median Percentage Change During Treatment, Interquartile range (Q1, Q3)</td>
<td>–41.9 (–72.4, –1.3)</td>
<td>–37.2 (–63.8, –5.6)</td>
<td>–17.2 (–37.1, 0.9)</td>
</tr>
<tr>
<td>Comparison over Placebo</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Estimated Median Difference (CI)*</td>
<td>–21.6 (–34.8, –6.7)</td>
<td>–19.2 (–31.2, –7.7)</td>
<td></td>
</tr>
<tr>
<td>p-value by Wilcoxon rank-sum test</td>
<td>0.0047</td>
<td>0.0016</td>
<td></td>
</tr>
</tbody>
</table>

Source: CSR Table 8.4.1.1-1, confirmed by FDA statistical reviewer
*based on Hodges-Lehmann estimator
CANNABIDIOL (EPIDIOLEX)

- Statistically significant differences between each CBD group vs. placebo

Table 2: Analyses of the Secondary Endpoints from Study 1414 (LOS)

<table>
<thead>
<tr>
<th>Variable</th>
<th>CBD 20 mg/kg/day (N=75)</th>
<th>CBD 10 mg/kg/day (N=73)</th>
<th>Placebo (N=76)</th>
</tr>
</thead>
<tbody>
<tr>
<td>% 50% Reduction in Drop Seizure Frequency</td>
<td>30 (39.5)</td>
<td>26 (35.6)</td>
<td>11 (14.5)</td>
</tr>
<tr>
<td>Odds Ratio (95% CI)</td>
<td>3.9 (1.8, 8.5)</td>
<td>3.3 (1.5, 7.3)</td>
<td></td>
</tr>
<tr>
<td>p-value by CMH test</td>
<td>0.0006</td>
<td>0.0300</td>
<td></td>
</tr>
<tr>
<td>Percentage Change from Baseline in Total Seizure Frequency during Treatment Period</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median Percentage Change During Treatment</td>
<td>-38.4</td>
<td>-36.4</td>
<td>-18.5</td>
</tr>
<tr>
<td>Estimated Median Difference (95% CI)</td>
<td>-18.8 [-31.8, -4.4]</td>
<td>-19.5 [-30.4, -7.5]</td>
<td></td>
</tr>
<tr>
<td>p-value by Wilcoxon rank-sum test</td>
<td>0.0091</td>
<td>0.0013</td>
<td></td>
</tr>
<tr>
<td>Subject/Caregiver Global Impression of Change Score at the Last Visit</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>3.0</td>
<td>3.2</td>
<td>3.6</td>
</tr>
<tr>
<td>Odds Ratio (95% CI)</td>
<td>1.6 (1.0, 2.3)</td>
<td>2.6 (1.4, 4.7)</td>
<td></td>
</tr>
<tr>
<td>p-value by Logistic Regression</td>
<td>0.0439</td>
<td>0.0020</td>
<td></td>
</tr>
</tbody>
</table>

Source: FDA clinical/statistical review
*based on Hodges-Lehmann estimator, confirmed by FDA statistical reviewer

CANNABIDIOL (EPIDIOLEX)

- MOA – unknown
- AE – somnolence (25%), decreased appetite (22%), diarrhea (20%), serum transaminase elevation (16%)
- Drug interactions
  - Cannabidiol is metabolized by CYP3A4, 2C19, UGT1A7, 1A9, 2B7
  - Moderate or strong 3A4 or 2C19 inhibitors can increase cannabidiol levels; inducers can decrease cannabidiol levels and efficacy
  - Cannabidiol is a potential inhibitor of UGT1A9 and 2B7, and CYP2C8, 2C9, 2C19
    - Cannabidiol can inhibit metabolism of clobazam and increase levels 3 fold
**CANNABIDIOL (EPIDIOLEX)**

- **Dose**
  - Supplied in 100 ml bottles containing 100 mg/ml
  - Starting dosage is 2.5 mg/kg twice daily
  - After one week the dosage can be increased to a maintenance dose of 5 mg/kg twice daily
  - As tolerated can increase to a maximum of 10 mg/kg twice daily
  - Reduce dose in hepatic impairment
  - Taking with high fat/high-calorie meal can increase maximum serum concentration of the drug 5-fold

One month treatment cost estimates range from $1,000-3,000/month

**DRONABINOL (SYNDROS)**

- Last year the FDA approved a new liquid formulation of dronabinol
- Same indications as Marinol
  - Anorexia associated with weight loss in patients with AIDS
  - Nausea and vomiting associated with cancer chemotherapy in patients who did not respond adequately to conventional treatment
- Bioavailability compared to Marinol
  - Dronabinol oral soln (Syndros) 4.25 mg is bioequivalent to dronabinol capsule (Marinol) 5 mg
- **Dose** (available as a 5 mg/ml oral solution)
  - 2.1 mg orally twice daily, one hour before lunch and dinner for anorexia
  - N/V – 4.2 mg/m², administered 1-3 hours prior to chemotherapy, then every 2-4 hours after chemotherapy, for a total of 4-6 doses/day. Administer first dose on an empty stomach.

Syndros costs about $2,000/month. Anticipated sales about $400 million/year
EFFICACY OF DRONABINOL IN HIV WASTING/ANOREXIA

- Efficacy – 10 studies of HIV wasting syndrome using dronabinol (Marinol)
  - Weight gain ranged from -2.0 to 3.2 kg (placebo weight change was -0.7 to 1.1 kg)
  - Dronabinol 2.5 mg po bid (-2.0 kg) vs. megestrol acetate 750 mg po qd (6.5 kg) (p=0.0001)
  - No studies on dronabinol oral solution in terms of efficacy (all bioequivalence)

- Efficacy of dronabinol in cancer-cachexia/anorexia (Marinol)
  - Open, dose-ranging studies evaluated on appetite stimulation in cancer patients
  - No significant weight gain was observed, but reduction in rate of weight loss and increased appetite scores were observed.
  - “Borderline” effect on mood (“If you’re happy and you know it….eat a cookie?”)

SUFENTANIL (DSUVIA) — WOW! HOT POTATO!

- Indication
  - Sufentanil, an opioid agonist, is indicated for use in adults in a certified medically supervised healthcare setting, such as hospitals, surgical centers, and emergency departments, for the management of acute pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate. Includes battlefield injuries.
  - NOT for home use, or use in children. DC treatment before leaving medical facility.
  - NOT for use > 72 hours, only to be administered by a healthcare provider.
**SUFENTANIL (DSUVIA) — WOW! HOT POTATO!**

- Dose – 30 mcg SL as needed with a minimum of one hour between doses
- Do not exceed 12 tablets in 24 hours
- Do not DC abruptly in an opioid-tolerant patient
- AE – nausea, headache, vomiting, dizziness, hypotension
- Tmax ~ 1 hour
  - Median time to meaningful pain relief ~ 54 minutes; 22% required rescue opioid

---

**DIRECTIONS FOR USE**

1. Only when ready to administer the medication, TEAR OPEN the notched pouch across the top. The pouch contains one clear plastic SDA with a single blue-colored tablet housed in the tip, and an oxygen absorber packet. See Figure 1.

2. REMOVE the white Lock from the green Pusher by squeezing the sides together and detaching from Pusher. See Figure 2.

3. TELL the patient to open their mouth and touch their tongue to the roof of their mouth if possible.

4. REST the SDA lightly on the patient’s lower teeth or lips. See Figure 3.

5. PLACE the SDA tip under the tongue and aim at the floor of the patient’s mouth or sublingual space. See Figure 3.

6. GENTLY DEPRESS the green Pusher to deliver the tablet to the patient’s sublingual space. See Figure 3.

7. VISUALLY CONFIRM tablet placement in the sublingual space. See Figure 4.

NOTE: If tablet is NOT in the patient’s mouth, it is important to retrieve and dispose of the tablet according to institutional CII waste procedures.

8. DISCARD the used SDA in biohazard waste after administration.
SO WHAT’S THE SITCH WITH SUFENTANIL?

• 10 times more potent than fentanyl
• 500-1,000 more potent than morphine
• MAJOR concerns about Dsuvia contributing to the opioid epidemic through abuse and diversion
  • “1,000 more potent than morphine = 1,000 times more likely to be abused and 1,000 times more likely to kill.”
• Community pharmacies will not stock this opioid
• Useful in patients where you cannot establish IV access

NEW DOSAGE FORM: SYMPAZAN (CLOBAZAM)

• Thin and berry-flavored, SYMPAZAN is taken without water, adheres to the tongue, and dissolves to deliver clobazam. 5, 10, 20 mg films.
• Indication – benzodiazepine indicated to treat seizures associated with Lennox-Gastaut Syndrome in patients ≥ 2 years old. Administered twice daily.

Sixty 10 mg films ~ $1,600
NEW DOSAGE FORM - APADAZ

- Benzhydrocodone/acetaminophen - 6.12 mg/325 mg
- CII indicated for acute severe pain (not to > 14 days)
- Initial dose, 1-2 tablets q4 or q6h prn, not to exceed 12 tablets/24 hours
- Two week supply = $245; two week supply Vicodin = $35

New Dosage Form - Cassipa

- New/higher dosage strength (16 milligrams/4 milligrams) of buprenorphine and naloxone sublingual film

NEW DOSAGE FORM – QMIIZ ODT

- Meloxicam orally disintegrating tablet
- 7.5 or 15 mg once daily

New Dosage Form – Tiglutik

- Riluzole oral suspension (5 mg/ml)
- Dose – 50 mg twice daily, every 12 hours
- Take at least 1 hour before or two hours after a meal
NEW DOSAGE FORM - CONSENSI

• Combo product – amlodipine/celecoxib
• We can raise your BP, but we can lower it too!!
• 2.5/200, 5/200, 10/200 mg once daily

New Dosage Form – Journay PM

• Delayed- and extended-release methylphenidate indicated for ADHD in patients 6 years and older
• Available as 20, 40, 60, 80, 100 mg once daily in the evening

NEW DOSAGE FORM — KAPSPARGO SPRINKLE

• Metoprolol extended-release capsule
• 25, 50, 100, 200 mg
• Swallow whole. If difficulty swallowing cap, may open and sprinkle contents over a teaspoonful of soft food (e.g., applesauce, yogurt, pudding) and consume mixture within 60 mins; or, can give via NG tube (mix contents with 15 mL of water first).
• Initially 100 mg once daily.
• May increase at 1-week intervals; max 400 mg/day. Reduce dose gradually over 1–2 weeks.
NEW DOSAGE FORM — PERSERIS

- Risperidone, an atypical antipsychotic indicated for the treatment of schizophrenia in adults.
- Now available as an extended-release injectable suspension, 90 mg and 120 mg.
- Dose – establish oral risperidone dose
- Initiate Perseris at 90 or 120 mg, once a month
- Administer in abdomen by healthcare professional.

OBSTETRICS/GYNECOLOGY

<table>
<thead>
<tr>
<th>Generic</th>
<th>Trade</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Segesterone acetate and ethinylestradiol-vaginal system</td>
<td>Annovera</td>
<td>For the prevention of pregnancy</td>
</tr>
<tr>
<td>Estradiol and progesterone</td>
<td>Bijuva</td>
<td>For the treatment of moderate to severe vasomotor symptoms due to menopause</td>
</tr>
<tr>
<td>Estradiol vaginal inserts</td>
<td>Imvexxy</td>
<td>For the treatment of moderate to severe dyspareunia, a symptom of vulvar and vaginal atrophy, due to menopause</td>
</tr>
<tr>
<td>Elagolix</td>
<td>Orilissa</td>
<td>For the management of moderate to severe pain associated with endometriosis</td>
</tr>
</tbody>
</table>
ELAGOLIX SODIUM (ORILISSA)

• A nonpeptide small molecule GnRH receptor antagonist
• Indication – Management of moderate to severe pain associated with endometriosis
• MOA – Inhibits endogenous GnRH signaling by binding, competitively to GnRH receptors in the pituitary gland. Suppresses luteinizing hormone and follicle-stimulating hormone, leading to decreased blood concentrations of the ovarian sex hormones, estradiol and progesterone.
• Response rate 46-76% vs. placebo (20%) (dysmenorrhea and pain)

ELAGOLIX SODIUM (ORILISSA)

• Reduction in estrogen is associated with a dose- and duration-dependent decrease in bone mineral density.
• Contraindicated in osteoporosis, pregnant women
• AE – hot flushes or night sweats (24%), headache (17%), nausea (11%), insomnia (6%), mood swings (6%), amenorrhea (4%), depression (3%) – all more likely at higher dose
• Dose – 150 mg once a day (up to 24 months)
  • Dyspareunia – up to 200 mg twice a day, up to 6 months
• Involved in many drug interactions

About $900/month for lower dose
### Oncology

<table>
<thead>
<tr>
<th>Generic</th>
<th>Trade</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calaspargase pegol</td>
<td>Asparlas</td>
<td>For the treatment of acute lymphoblastic leukemia in adults and young adults</td>
</tr>
<tr>
<td>Encorafenib</td>
<td>Braftovi</td>
<td>For the treatment of unresectable or metastatic melanoma with a BRAFV600E or BRAFB600K mutation</td>
</tr>
<tr>
<td>Binimetinib</td>
<td>Mektovi</td>
<td>For the treatment of chronic lymphocytic leukemia, small lymphocytic lymphoma or follicular lymphoma</td>
</tr>
<tr>
<td>Duvelisib</td>
<td>Copiktra</td>
<td>For the treatment of newly diagnosed acute myeloid leukemia in adults 75 years of age or older</td>
</tr>
<tr>
<td>Glasdebig</td>
<td>Daurismo</td>
<td>For the treatment of blastic plasmacytoid dendritic cell neoplasm in adults and pediatrics</td>
</tr>
<tr>
<td>Tagraxofusp</td>
<td>Elzonris</td>
<td>For the treatment of prostate cancer</td>
</tr>
</tbody>
</table>

### Oncology

<table>
<thead>
<tr>
<th>Generic</th>
<th>Trade</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cemiplimab</td>
<td>Libtayo</td>
<td>For the treatment of cutaneous squamous cell carcinoma</td>
</tr>
<tr>
<td>Lorlatinib</td>
<td>Lorbrena</td>
<td>For the treatment of ALK-positive metastatic non-small cell lung cancer</td>
</tr>
<tr>
<td>Moxetumomab pasudotox</td>
<td>Lumoxiti</td>
<td>For the treatment of relapsed or refractory hairy cell leukemia</td>
</tr>
<tr>
<td>Lutetium Lu 177 dotate</td>
<td>Lutathera</td>
<td>For the treatment of gastroenteropancreatic neuroendocrine tumors</td>
</tr>
<tr>
<td>Mogamulizumab</td>
<td>Poteligeo</td>
<td>For the treatment of mycosis fungoides or Sezary syndrome</td>
</tr>
<tr>
<td>Talazoparib</td>
<td>Talzenna</td>
<td>For the treatment of deleterious germline BRCA-mutated HER2-negative locally advanced or metastatic breast cancer</td>
</tr>
<tr>
<td>Ivosidenib</td>
<td>Tibsovo</td>
<td>For the treatment of acute myeloid leukemia with a susceptive IDH1 mutation</td>
</tr>
</tbody>
</table>
ONCOLOGY

<table>
<thead>
<tr>
<th>Generic</th>
<th>Trade</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Larotrectinib</td>
<td>Vitrakvi</td>
<td>For the treatment of solid tumors that have a neurotrophic receptor tyrosine kinase (NTRK) gene fusion</td>
</tr>
<tr>
<td>Dacomitinib</td>
<td>Vizimpro</td>
<td>For the treatment of metastatic non-small cell lung cancer</td>
</tr>
<tr>
<td>Gilteritinib</td>
<td>Xospata</td>
<td>For the treatment of acute myeloid leukemia with a FLT3 mutation</td>
</tr>
</tbody>
</table>

APALUTAMIDE (ERLEADA)

- **Indication** – An androgen receptor inhibitor, indicated for the treatment of patients with non-metastatic castration-resistant prostate cancer.
- **Dose** – 240 mg (four 60 mg tablets) orally once daily; swallow whole. Can take with or without food.
  - Patients should also receive a gonadotropin-releasing hormone (GnRH) analog concurrently or should have had bilateral orchiectomy.
- **Warnings** – falls (16%), fractures(12%), seizures (0.2%)
- **AE > 10%** - fatigue, hypertension, rash, diarrhea, nausea, weight decreased, arthralgia, falls, hot flush, decreased appetite, fracture, peripheral edema.

<table>
<thead>
<tr>
<th></th>
<th>Erleada</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metastasis free survival</td>
<td>40.51 months</td>
<td>16.20 months</td>
</tr>
<tr>
<td>Time to metastasis</td>
<td>40.51 months</td>
<td>16.59 months</td>
</tr>
<tr>
<td>Progression-Free survival</td>
<td>40.51 months</td>
<td>14.72 months</td>
</tr>
</tbody>
</table>

$12,000/month
OSIMERTINIB (TAGRISSO)

- **Indication** – A kinase inhibitor indicated for:
  - The first-line treatment of patients with metastatic NSCLC whose tumors have epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 L858R mutations, as detected by an FDA-approved test
  - The treatment of patients with metastatic EGRF T790M mutation-positive NSCLC, as detected by an FDA-approved test, whose disease has progressed on or after EGFR TKI therapy
  - NOT chemotherapy or immune therapy
  - Dose – 80 mg by mouth once daily, with or without food

Osimertinib (Tagrisso) Warnings

- Interstitial lung disease
- QTc interval prolongation
- Cardiomyopathy
- Keratitis
- Embryo-fetal toxicity

Adverse Effects > 20%

- Diarrhea
- Rash
- Dry skin
- Nail toxicity
- Stomatitis
- Fatigue
- Decreased appetite

$15,000/month

<table>
<thead>
<tr>
<th>Efficacy Parameter</th>
<th>Tagrisso</th>
<th>Gefitinib or Erlotinib</th>
</tr>
</thead>
<tbody>
<tr>
<td>PFS events</td>
<td>49%</td>
<td>74%</td>
</tr>
<tr>
<td>Progressive disease</td>
<td>45%</td>
<td>69%</td>
</tr>
<tr>
<td>Death</td>
<td>4%</td>
<td>5%</td>
</tr>
<tr>
<td>Median PFS in months</td>
<td>18.9</td>
<td>10.2</td>
</tr>
<tr>
<td>Overall response rate</td>
<td>77%</td>
<td>63, 74%</td>
</tr>
<tr>
<td>Complete response</td>
<td>2%</td>
<td>1%</td>
</tr>
<tr>
<td>Partial response</td>
<td>75%</td>
<td>68%</td>
</tr>
<tr>
<td>Duration of response in months</td>
<td>17.6</td>
<td>9.6</td>
</tr>
<tr>
<td>Generic</td>
<td>Trade</td>
<td>Indication</td>
</tr>
<tr>
<td>-------------------------</td>
<td>----------</td>
<td>-----------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Cenegermin</td>
<td>Oxervate</td>
<td>For the treatment of neurotrophic keratitis</td>
</tr>
<tr>
<td>Netarsudil dimesylate</td>
<td>Rhopressa</td>
<td>Reduction of elevated IOP in patients with open-angle glaucoma or ocular hypertension</td>
</tr>
<tr>
<td>Voretigene neparvovec</td>
<td>Luxturna</td>
<td>First gene therapy to target inherited retinal dystrophy</td>
</tr>
</tbody>
</table>

**PHARMACOLOGY**

<table>
<thead>
<tr>
<th>Generic</th>
<th>Trade</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lofexidine</td>
<td>Lucemyra</td>
<td>For the mitigation of opioid withdrawal symptoms to facilitate abrupt opioid discontinuation in adults</td>
</tr>
</tbody>
</table>

**NETARSUDIL DIMESYLATE (RHOPRESSA)**

- Ophthalmic solution indicated for the reduction of intraocular pressure in patients with open-angle glaucoma or ocular hypertension
- Unique MOA – Rho kinase inhibitor – reduces IOP by increasing the outflow of aqueous humor through the trabecular meshwork
- Dose – 0.02% per day in the evening (5 minutes apart from other ophthalmic medications)
- Efficacy ≤ ophthalmic timolol (equal up to baseline IOP of 25 mmHg)
- AE – conjunctival hyperemia (53%), corneal verticillate (opacities), instillation-site pain, conjunctival hemorrhage (20% for each)

About $260/month
NEW DOSAGE FORM — XELPROS

- Latanoprost, prostaglandin F\textsubscript{2α} analogue indicated for reduction of elevated intraocular pressure in patients with open-angle glaucoma, or ocular hypertension.
- Now available as an ophthalmic suspension
- Dose is one drop in the affect eye(s) once daily in the evening
- AE > 5% - eye pain/stinging, ocular hyperemia, conjunctival hyperemia, eye discharge, growth of eyelashes, eyelash thickening.

<table>
<thead>
<tr>
<th>Generic latanoprost/month</th>
<th>Xelpros/month</th>
</tr>
</thead>
<tbody>
<tr>
<td>$13.00</td>
<td>$60.00</td>
</tr>
</tbody>
</table>

It’s a SPEED-DATING tip!

- Researchers in Canada evaluated 214 patients with primary open-angle glaucoma who received a prostaglandin analog (e.g., latanoprost [Xalatan]) for at least six months.
- Half the group was randomized to discontinue the prostaglandin analog, and intraocular pressure was compared with the control group at 1, 3 and 6 weeks later.
- In the group who discontinued therapy, their intraocular pressure increased somewhat, but was significantly lower than their baseline pressure.
- This effect was seen in some patients for up to a year.
- This data may reassure patients with a prognosis of a few months that a prostaglandin analog may be safely discontinued without causing harm.

LOFEXIDINE (LUCEMYRA)

- A central alpha-2 adrenergic agonist with properties similar to those of clonidine
- First nonopioid agent approved for mitigation of opioid withdrawal symptoms to facilitate abrupt opioid discontinuation in adults
- MOA – binds to receptors on adrenergic neurons, reducing the release of NE and decreasing sympathetic tone
- Reduces, may not completely prevent, withdrawal symptoms
- Recommended treatment duration is up to 14 days

LOFEXIDINE (LUCEMYRA)

- Efficacy – two trials. Outcomes included:
  - SOWS-Gossop (Short Opiate Withdrawal Scale of Gossop)
    - Mean SOWS-Gossop was lower with lofexidine vs. placebo
  - Proportion of patients who completed treatment period
    - 41% with lofexidine vs. 28% placebo patients finished 7 day treatment
    - 49% with lofexidine vs. 33% placebo patients within 5 day treatment
  - AE – insomnia (50%; vs. 48% with placebo), hypotension (30%), orthostatic hypotension (29%), bradycardia (24%), dizziness (19%), sedation (13%), somnolence (11%), dry mouth (10%). Caution with cardiac patients.
  - Dose – 0.54 mg four times daily during peak withdrawal symptoms (first 5-7 days after last use of opioid); tx may continue up to 14 days (taper down)

96 of the 0.18 mg tablets (8 days treatment) ~ $2,000.00 ($3,500 for 14 days)
PULMONARY/RESPIRATORY DISEASES

<table>
<thead>
<tr>
<th>Generic</th>
<th>Trade</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tezacaftor/ivacaftor</td>
<td>Symdeko</td>
<td>For the treatment of cystic fibrosis</td>
</tr>
<tr>
<td>Revefenacin</td>
<td>Yupelri</td>
<td>For the maintenance treatment of chronic obstructive pulmonary disease</td>
</tr>
</tbody>
</table>

Rheumatology

<table>
<thead>
<tr>
<th>Generic</th>
<th>Trade</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baricitinib</td>
<td>Olumiant</td>
<td>For the treatment of moderate to severe rheumatoid arthritis with inadequate response to TNF antagonist therapies</td>
</tr>
</tbody>
</table>

Urology

<table>
<thead>
<tr>
<th>Generic</th>
<th>Trade</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Desmopressin acetate</td>
<td>Nocdurna</td>
<td>For the treatment of nocturia due to nocturnal polyuria</td>
</tr>
</tbody>
</table>

REVEFENACIN (YUPELRI)

- Indication – An anticholinergic indicated for the maintenance treatment of patients with COPD.
- Dosage – 175 mcg vial (3 ml) once daily by nebulizer
- Warnings
  - Do not use in acutely deteriorating COPD or to treat acute symptoms
  - If paradoxical bronchospasm occurs, DC medication
  - Worsening of narrow angle glaucoma may occur
  - Worsening of urinary retention may occur
- AE – cough, nasopharyngitis, URI, headache, back pain
THOSE DARNED INHALERS...

<table>
<thead>
<tr>
<th>Drug</th>
<th>Formulation</th>
<th>Delivery Device</th>
<th>Usual Adult Dosage</th>
<th>Cost/Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aclidinium (Tudorza Pressair)</td>
<td>400 mcg/inh</td>
<td>DPI</td>
<td>1 inh bid</td>
<td>$351.80</td>
</tr>
<tr>
<td>Glycopyrrolate (Seebri Neohaler)</td>
<td>15.6 mcg/cap</td>
<td>DPI</td>
<td>1 inh bid</td>
<td>$394.20</td>
</tr>
<tr>
<td>Glycopyrrolate (Lonhala Magnair)</td>
<td>25 mcg/ml soln</td>
<td>Nebulizer</td>
<td>25 mcg bid</td>
<td>$1,132.80</td>
</tr>
<tr>
<td>Revefenacin (Yupeli)</td>
<td>175 mcg/3 ml soln</td>
<td>Nebulizer</td>
<td>175 mcg once/day</td>
<td>$1030.00</td>
</tr>
<tr>
<td>Tiotropium (Spiriva Handihaler)</td>
<td>18 mcg/cap</td>
<td>DPI</td>
<td>18 mcg once/day</td>
<td>$429.50</td>
</tr>
<tr>
<td>Tiotropium (Spiriva Respimat)</td>
<td>2.5 mcg/inh</td>
<td>SMI</td>
<td>2 inh once/day</td>
<td>$429.50</td>
</tr>
<tr>
<td>Umeclidium (Incruse Ellipta)</td>
<td>62.5 mcg/inh</td>
<td>DPI</td>
<td>1 inh once/day</td>
<td>$333.80</td>
</tr>
<tr>
<td>Ipratropium/albuterol</td>
<td>0.5 mg/3 mg/vial</td>
<td>Nebulizer</td>
<td>1 inh q4h while awake</td>
<td>$75</td>
</tr>
</tbody>
</table>

NEW DOSAGE FORM – PRIMATENE MIST

- Heaven help us – it’s BAAAAACCKKKK
- Epinephrine inhaler – Primatene Mist
- Back on the OTC market
- Originally used chlorofluorocarbons (CFCs) to propel the medication into the lungs. Reformulated with hydrofluoroalkane (HFA) propellants.
- This metered-dose inhaler is approved only for those who have been diagnosed with asthma by a healthcare provider.
PRESCRIPTION OPIOID COUGH/COLD MEDICATIONS

• FDA requiring safety labeling changes for products containing codeine or hydrocodone to limit the use of these products to adults 18 years or older due to risks in children.
• Risks of slowed or difficult breathing, misuse, abuse, addiction, overdose and death outweigh their benefit in patients younger than 18.

BARICITINIB (OLUMIANT)

• Second JAK inhibitor to be approved for tx of rheumatoid arthritis (joining tofacitinib [Xeljanz])
• Treatment of adult patients with moderately to severely active RA with inadequate response to one or more TNF antagonist therapies
  • Palliative (NSAIDs, steroids)
  • Disease-modifying anti-rheumatic drugs (DMARDs)
    • Conventional – methotrexate
    • Biologic – TNF inhibitors (adalimumab [Humira], certolizumab [Cimzia], etanercept [Enbrel], golimumab [Simponi], infliximab [Remicade])
    • Janus kinase (JAK) enzymes are intracellular enzymes that transmit signals arising from cytokine or growth factor-receptors interactions on the cellular membrane to influence cellular processes of hematopoiesis and immune cell function. Baricitinib is a JAK inhibitor.
BARICITINIB (OLUMIANT)

- In clinical trial, patients who failed methotrexate received baricitinib.
  - 66% of baricitinib patients achieved an ACR20 response at week 12, compared with 39% of placebo patients
- In clinical trial, patients who failed or didn’t tolerate a TNF inhibitor received baricitinib
  - 49% achieved an ACR20 response at week 12, vs. 27% placebo patients
- Precautions/Contraindications
  - Do not use in combination with biologic DMARDs or strong immunosuppressants
  - Do not initiate therapy in patients with absolute lymphocyte count < 500 cell/mm3, ANC < 1,000 cell/mm3 or hemoglobin < 8 g/dl
  - Use not recommended with GFR < 60 ml/min or severe hepatic impairment
  - Caution in patients at increased risk for GI perforations; hematologic toxicity possible; lymphoma possible
  - May increase liver enzymes; increased risk for infections; dose dependent increase in lipids
  - Thrombosis (including DVT, PE, arterial thrombosis) have been observed
  - Do not administer live vaccines
- Dose – 2 mg by mouth once daily

Cost is $82 per DAY

Health Care Provider Clinical Practice Guidelines - 2018 Year in Review

- COPD
- Arterial hypertension clinical practice GL
- Idiopathic pulmonary fibrosis
- Antimicrobial prophylaxis for cancer pts
- Palliative care clinical practice guidelines
- Adult chronic diarrhea clinical practice GL
- Biologic DMARD safety guidelines
- Alzheimer’s disease clinical practice GL
- Alcohol-related liver disease clinical GL
- Neuropathic pain p’cox clinical practice GL
- Deprescribing BZD for insomnia GL
- Cirrhosis clinical practice guidelines
- Crohn disease clinical practice guidelines
- Diarrhea clinical practice guidelines
- Urinary incontinence clinical practice GL
- Multiple sclerosis clinical practice GL
- Bipolar disorder clinical practice GL
- Hepatitis E clinical practice guidelines
I’M EXHAUSTED....WHAT’S IN STORE FOR 2019??

• 5 potential BIG HITS in 2019
  • Gene therapy for Duchenne muscular dystrophy (mutation on exon 53) – golodirsen – probably will be close to $300,000 per year
  • New option for multiple sclerosis – siponimod – first oral disease-modifying therapy for secondary progressive multiple sclerosis
  • An oral insulin adjunct for type 1 diabetes – sotagliflozin
  • Injectable for psoriasis – risankizumab for plaque psoriasis, an autoimmune disease
  • A longer-duration drug for a rare blood disorder – paroxysmal nocturnal hemoglobinuria (PNH) – Ultomiris – every 8 weeks (instead of every 2 weeks) - $458,000/year!