New Drugs and Drug News of 2017

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Home Study Webcast

4 Slides Per Page

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New Drugs and Drug News of 2017

ACTIVITY DESCRIPTION

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

TARGET AUDIENCE

The target audience for this activity is **pharmacists, pharmacy technicians** and **nurses** in hospital, community, and retail pharmacy settings.

LEARNING OBJECTIVES

After completing this activity, the **pharmacist** will be able to:

- Review the approved indication, common adverse effects and drug interactions of selected new drugs approved by the FDA in 2017
- For each new medication approved in 2017, describe the burden-to-benefit ratio of therapy.
- Analyze important drug alerts by the FDA (Public Health Advisories) and implications for patient care.

After completing this activity, the **pharmacy technician** will be able to:

- Review the approved indication, common adverse effects and drug interactions of selected new drugs approved by the FDA in 2017
- For each new medication approved in 2017, describe the burden-to-benefit ratio of therapy.
- Analyze important drug alerts by the FDA (Public Health Advisories) and implications for patient care.

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Knowledge-Based Home Study Webcast

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ABOUT THE AUTHOR

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Dr. McPherson has maintained a practice in hospice and palliative care (local and national) and ambulatory care her entire career. Dr. McPherson teaches extensively in the Doctor of Pharmacy curriculum on pain management and end of life care, including didactic and experiential content. She also developed one of the first and few palliative care pharmacy residencies in the U.S.

Dr. McPherson serves on the Board of the Hospice Network of Maryland, and was founding president of the American Society of Pain Educators. McPherson is a Fellow in the American Society of Health-Systems Pharmacists, the American Pharmacists Association, the American Society of Consultant Pharmacists and the American Society of Pain Educators. She is Board Certified in Pharmacotherapy, a Certified Diabetes Educator and a Certified Pain Educator. She has received many honors for her work, including the American Pharmacists Association Distinguished Achievement Award in Specialized Practice, the Maryland Pharmacists Association Innovative Practice Award, and the Maryland Society of Health-Systems Pharmacists W. Purdum Lifetime Achievement Award. Dr. McPherson has received many awards for teaching including the Presidential Citation from the Hospice and Palliative Nurses Association, Professor of the Year many times from the School of Pharmacy, University of Maryland Baltimore Founder's Week Teacher of the Year and the Robert Chalmers Distinguished Educator Award from the American Association of Colleges of Pharmacy. She has written four books, including "Demystifying Opioid Conversion Calculations: A Guide for Effective Dosing," and many book chapters and peer-reviewed articles on pain management, palliative care, and other topics.

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New Drugs and Drug News of 2017

Faculty: Mary Lynn McPherson, PharmD, MA, BCPS, CPE

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Objectives

- At the end of this presentation the participant will be able to:
  - Review the approved indication, common adverse effects and drug interactions of selected new drugs approved by the FDA in 2017.
  - For each new medication approved in 2017, describe the burden-to-benefit ratio of therapy.
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Novel Drug Approvals

CDER's Novel Drug Approvals of 2017

CDER's novel drug approvals for 2017 are listed below.* See CDER's Novel Drug Approvals for 2017 on the FDA website for the approval dates, non-proprietary names, and what each drug is used for.

Aliqopa	Brineura	Imfinzi	Ocrevus	Solosec	Vosevi
Alunbrig	Calquence	Ingrezza	Ozempic	Steglatro	Vyzulta
Austedo	Dupixent	Kevzara	Parsabiv	Symproic	Xadago
Bavencio	Emflaza	Kisqali	Prevymis	Tremfya	Xermelo
Baxdela	Fasenra	Macrilen	Radicava	Trulance	Xepi
benznidazole**	Giapreza	Mavyret	Rhopressa	Tymlos	Zejula
Besponsa	Hemlibra	Mepsevii	Rydapt	Vabomere	
Bevyxxa	Idhifa	Nerlynx	Siliq	Verzenio	

* This information is accurate as of December 31, 2017. In rare instances, it may be necessary for FDA to change a drug's NME designation or the status of its application as a novel BLA. For instance, new information may become available which could lead to a reconsideration of the original designation or status. If changes must be made to a drug's designation or the status of an application as a novel BLA, the Agency intends to communicate the nature of, and the reason for, any revisions as appropriate.
** Product approved with no trade name.

JCM591976.pdf

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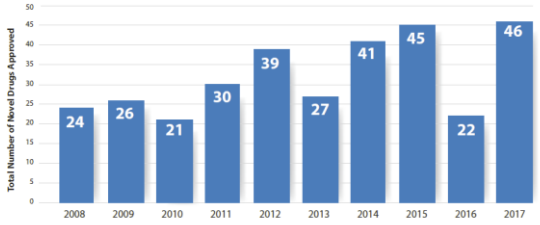
Novel Drug Approvals 2008-2017

CDER's Annual Novel Drug Approvals: 2008 - 2017

In 2017, CDER approved 46 novel drugs. The ten-year graph below shows that from 2008 through 2016, CDER has averaged about 31 novel drug approvals per year.



https://www.fda.gov/downloads/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/ReportsBudgets/UCM591976.pdf

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Examples of novel drugs for rare diseases

- **Cerliponase alfa (Brineura)**
  - A treatment for a specific form of **Batten disease** – a rare disease that can cause progressive neurological impairments, including seizures, visual problems/blindness, personality and behavior changes, dementia, and the loss of the ability to walk, talk and communicate.
- **Emicizumab (Hemlibra)**
  - For the prevention of bleeding or to reduce the frequency of bleeding episodes in patients with **hemophilia A** who have developed antibodies called Factor VIII inhibitors. This is the first non-blood product approved for this condition

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Safinamide mesylate (Xadago)

- Third MAO-B inhibitor in US for Parkinson's disease (reversible)
  - Selegiline (Eldepryl), rasagiline (Azilect) – both irreversible
- Inhibiting MAO-B reduces the catabolism of dopamine
  - Increased dopamine in the brain
- Indicated as adjunct treatment to levodopa/carbidopa in PD who are experiencing "off" episodes
- In clinical trials, significantly increased "on" time without troubling dyskinesias, and reduced "off" time (-0.56 hours/day)

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Safinamide mesylate (Xadago)

- Adverse effects include:
  - Dyskinesia (17%)
  - Increased serum alanine aminotransferase (7% to above the ULN)
  - Falls (6%); Nausea (6%); Insomnia (4%)
- Other noted effects with MAO-B inhibitors:
  - Sleep attacks/sudden onset of sleep and/or fallen asleep suddenly
  - Impulse control and compulsive behaviors (gambling, spending $$, binge eat, increased sexual urges)
  - Do not use if patient has a major psychotic disorder
  - May cause hypertension; avoid concurrent MAOI or linezolid

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Safinamide mesylate (Xadago)

- Other noted effects with MAO-B inhibitors:
  - Avoid foods containing a large amounts of tyramine
  - Avoid sympathomimetic medications (monitor for hypertension)
  - Risk of serotonin syndrome
    - SNRIs, TCAs, cyclobenzaprine, St. John's wort contraindicated
    - Concurrent use of meperidine, methadone, tramadol contraindicated
    - Concurrent use of dextromethorphan is contraindicated
    - Concurrent use with SSRI not recommended
- Reduce dose in moderate hepatic impairment; do not use with severe

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Safinamide mesylate (Xadago)

- **Advantages** as compared to rasagiline and selegiline
  - May be used in patients with renal impairment (compared with selegiline, which is not recommended in patients with severe renal impairment)
- **Disadvantages** as compared to rasagiline and selegiline
  - Has not been directly compared in clinical trials with comparable drugs
  - Labeled indications are more limited (compared with rasagiline, for which the labeled indications also include monotherapy and adjunctive therapy without levodopa)
  - Is contraindicated in patients with severe hepatic impairment
- Dose – 50 mg po qd; increase at 2 weeks to 100 mg po qd
  - Moderate hepatic impairment reduce to 50 mg po qd
  - $800/month

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Edaravone (Radicava)

- Indicated to slow the progression of ALS (Lou Gehrig disease)
  - A progressive neurodegenerative disease affecting 12-15,000 Americans
  - Approximately 5,000 patients diagnosed annually
  - Most patients die from respiratory failure in 3-5 years after symptom onset
- Riluzole (Rilutek) – FDA approved in 1995 for ALS
  - Acts by reducing glutamate release and reducing accumulation of this amino acid in nerve cell synapses
  - Prolongs survival on average by 3 months

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Edaravone (Radicava)

- Edaravone is an IV infusion
  - 60 mg as two consecutive 30 mg IV infusion bags over a total of 60 minutes (1 mg/min)
  - Initial treatment cycle is 60 mg once a day for 14 days
  - Followed by a 14 day drug-free period
  - In subsequent treatment cycles, a 60 mg dose is administered once a day for 10 days over of a 14-day period, followed by 14-day drug-free periods
- Adverse effects
  - Contusions (bruising, 15%), gait disturbance (13%), headache (10%)
  - Dermatitis (8%), eczema (7%)
  - Respiratory failure/disorder or hypoxia (6%)
  - Hypersensitivity reactions

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Edaravone (Radicava)

- Mechanism of action - unknown
- Study in Japan – 69 patients on edaravone; 68 on placebo
  - 90% were also on riluzole
  - ALS Functional Rating Scale (12 questions, 0-4 scale)
  - Decline in scores from baseline to 24 weeks
    - Edaravone patients (-5.01) vs. placebo (-7.50)
- Advantages
  - Slows the worsening of ALS symptoms
- Disadvantages
  - Prolongation of survival has not been demonstrated (unknown)
  - Is administered intravenously (riluzole is PO); $1300 a dose

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Valbenazine (Ingrezza)

- First drug approved for treatment of adult patients with tardive dyskinesia
  - Neurological disorder characterized by involuntary movements, usually of the mouth, lips, and tongue, and occasionally, by rapid movement of the arms and legs
  - Could include difficulty in speaking, swallowing, breathing
  - Most often in patients treated for long periods with older antipsychotic medications (phenothiazines, haloperidol); may occur after DC'ing tx
- Valbenazine – mechanism of action is unknown
  - Thought to be mediated through the reversible inhibition of vesicular monoamine transporter 2 (VMAT2)

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Valbenazine (Ingrezza)

- Effectiveness
  - Placebo-controlled trial in 234 patients with moderate-to-severe TD
  - Had underlying schizophrenia, schizoaffective disorder, or mood disorder
  - 85% were being treated with antipsychotic agents
- AIMS (Abnormal Involuntary Movement Scale) used to assess TD severity
  - Primary efficacy endpoint was mean change from baseline at 6 weeks
  - Difference seen at 6 weeks; at end of week 6 those on placebo were re-randomized to valbenazine
  - Follow-up continued through week 48, followed by 4 weeks off drug
  - AIMS score returned to baseline when medication stopped

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Valbenazine (Ingrezza)

- Similar to tetrabenazine – which has boxed warning on depression and suicidality
  - Patients with unstable psychiatric symptoms were excluded from trial
- Causes fetal harm, avoid with breast feeding
- Take with or without food
- Numerous drug interactions
  - Do not use with MAOIs (serotonin syndrome, reduced valbenazine effect)
  - Strong 3A4 inhibitors or 2D6 inhibitors increase serum level
  - Strong 3A4 inducers reduce concentration

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Valbenazine (Ingrezza)

- Adverse effects
  - Somnolence (11%), anticholinergic effects (5% - dry mouth, blurred vision)
  - Prolonged QTc (not clinically significant at usual dose)
- Initial dose if 40 mg po qd; increase in 1 week to 80 mg po qd
  - Continue 40 mg dose with moderate to severe hepatic impairment, or patients with known 2D6 poor metabolizers, or concurrent 2D6 inhibitors
- Cost is > $100,000/year; available through specialty pharmacies.
- Advantages – first drug demonstrated to be effective for TD
- Disadvantages – may prolong QT and risk arrhythmia; may interact with numerous drug interaction

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Deutetrabenazine (Austedo)

- Huntington disease – inherited neurologic disorder that results in progressive breakdown of nerve cells in the brain
- 30,000 people in US have Huntington disease, symptoms usually occur between 30 and 50 years old
  - Movement (chorea), cognitive, psychiatric manifestations
  - Chorea – involuntary jerking or writhing movements seen in 90% patients
- Deuterated form of tetrabenazine (Xenazine, approved in 2008)
- Approved for treatment of chorea associated with Huntington disease
- Mechanism – thought to reversibly inhibit the human VMAT2, resulting in decreased uptake of monoamines (DA, NE, 5HT, H)

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Deutetrabenazine (Austedo)

- Effectiveness
  - Placebo-controlled trial – primary efficacy endpoint was the Total Maximal Chorea Score (0-28)
    - Deutetrabenazine improves scores by 4.4 units from baseline (vs. 1.9 with placebo)
  - 51% patients self-rated as much improved or very much improved vs. 20% placebo; likely similar effectiveness to tetrabenazine
- Adverse effects
  - Increased risk of depression and suicidality
  - Contraindicated in hepatic impairment, patients on MAOI or reserpine
  - Somnolence (11%), diarrhea (9%), dry mouth (9%), fatigue (9%), UTI (7%), insomnia (7%)
  - Avoid alcohol due to cumulative sedating effects

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Deutetrabenazine (Austedo)

- Additional adverse effects
  - Parkinsonism, akathisia, agitation, restlessness, neuroleptic malignant syndrome, hyperprolactinemia, binding to melanin-containing tissues (e.g., in the eye)
  - Tetrabenazine (not deutetrabenazine) – warnings about hypotension and orthostasis, dysphagia, tardive dyskinesia
  - Both can cause QTc interval prolongation
  - May cause fetal harm
- Co-administration with 2D6 inhibitors increase systemic exposure to active metabolites by 3X

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Deutetrabenazine (Austedo)

- Recommended starting dose if 6 mg once a day with food
- Increase at weekly intervals by 6 mg/day to a tolerated dose that reduces chorea, up to a maximum recommended daily dosage of 48 mg (24 mg BID) (split daily doses > 12 mg into two doses)
  - Do not exceed 36 mg a day if given with 2D6 enzyme inhibitor
- Advantages (compared to tetrabenazine)
  - May be less likely to cause adverse effects
  - Administered less frequently for maintenance treatment (BID vs. TID)
- Disadvantages
  - As not been directly compared with tetrabenazine in clinical studies
  - $\geq$ $6,000/month (12 mg bid)

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Bezlotoxumab (Zinplava)

- *C. difficile* is an anaerobic Gram-positive bacillus that produces two toxins (A and B) and spores
- *C. difficile* can survive in the environment for long periods of time and can be spread by health care personnel
  - *Spores are highly resistant to alcohol-based hand sanitizers*
- Risk factors include systemic antibacterial therapy, > 65 years old, prior episodes of *C. diff* infection, immunocompromised, hypervirulent strains of *C. diff*

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Bezlotoxumab (Zinplava)

- Usual treatments include metronidazole, vancomycin (for more severe), fidaxomicin
- CDI can recur in up to 40% patients who were previously successfully treated for CDI
- Bezlotoxumab (Zinplava) – human monoclonal antibody that binds to *C. diff* toxin B and neutralizes its effect
  - Not an antibacterial
  - Single IV dose in conjunction with antibacterial treatment
  - Indicated to reduce recurrence of CDI in adult patients who are receiving antibacterial drug treatment of CDI and are at high risk of recurrence

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Bezlotoxumab (Zinplava)

- Two trials showed effectiveness
  - Single IV infusion of bezlotoxumab or placebo given to patients with CDI in addition to standard of care 10-14 day course of metronidazole, vancomycin or fidaxomicin
  - Sustained clinical response was defined as clinical cure of the presenting CDI episode and no recurrence through 12 weeks after infusion
- Trial 1 – bezlotoxumab vs. placebo was 60% vs. 55% - not SS
- Trial 2 - bezlotoxumab vs. placebo was 67% vs. 52% - was SS
- Dose is 10 mg/kg administered as an IV infusion over 60 minutes

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Bezlotoxumab (Zinplava)

- Adverse effects include:
  - Nausea (7%), pyrexia (5%), headache (4%)
  - Heart failure reported with bezlotoxumab (13%) vs. placebo (5%)
    - Patients with h/o CHF – higher death rate (20% vs. 13%) during 12 week study
- Advantages
  - May reduce recurrence of CDI
  - Unique MOA – binds to *C. Difficile* toxin B and neutralizes its effects
  - Single-dose treatment
- Disadvantages
  - Does not exhibit antibacterial action; not indicated for tx of CDI
  - Increased risk in patients with h/o CHF
  - Administered IV (comparable drugs are oral)
  - $4560.00/dose

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Betrixaban (Bevyxxa)

- Fourth orally administered anticoagulant – inhibits Factor Xa
  - **Rivaroxaban (Xarelto)** – Prophylaxis of DVT in patients undergoing knee or hip replacement surgery; treat and reduce risk of recurrence of DVT/PE, and reduce risk of stroke and systemic embolism in patients with NVAF
  - **Apixaban (Eliquis)** – Reduce risk of stroke and systemic embolism in NVAF; prophylaxis of DVT in knee/hip replacement surgery; treatment and reduction of risk of recurrence of DVT and PE after initial therapy
  - **Edoxaban (Savaysa)** – To reduce risk of stroke and systemic embolism in patients with NVAF; treatment of DVT and PE after 5-10 days of initial therapy with a parenteral anticoagulant

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Betrixaban (Bevyxxa)

- Betrixaban mechanism and indication
  - Blocks active site of Factor Xa; inhibits free factor Xa and prothombinase activity. No direct effect on platelet aggregation
  - Indicated for prophylaxis of venous thromboembolism (VTE) in adults patients hospitalized for an acute medical illness who are at risk for thromboembolic complications due to moderate or severe restricted mobility and other risk factors for VTE.
    - Many VTE events and related deaths occur in acutely ill medical patients, despite standard use of injectable enoxaparin and other heparins in the hospital
  - First anticoagulant indicated for in-hospital and extended-duration VTE prophylaxis in acutely ill medical patients

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Betrixaban (Bevyxxa)

- Efficacy – Betrixaban 35-42 days vs. enoxaparin 6-14 days to prevent VTE in patients hospitalized
  - Composite outcome – up to the 35 days visit of the occurrence of asymptomatic proximal DVT, symptomatic proximal or distal DVT, nonfatal PE, or VTE-related death
  - Betrixaban reduced composite outcome by 6.0% vs. placebo and enoxaparin 4.4%. Also reduced symptoms and death rate.
  - Major bleeding was 0.67% vs. 0.57% (placebo)
  - Discontinuation due to bleeding was 2.4% vs. 1.2% (placebo)
  - No specific antidote for betrixaban-induced bleeding
  - Other AE – clinically relevant nonmajor bleeding (2.45%), UTI (3%), constipation (3%), hypokalemia (3%)

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Betrixaban (Bevyxxa)

- Administer with food at the same time each day for 35-42 days
- Caution with P-gp inhibitors (amiodarone, azithryomycin, verapamil, ketoconazole, clarithromycin)
- Dose – initial single dose of 160 mg; followed by 80 mg po qd
  - With severe renal impairment, or P-gp inhibitor, initial single dose of 80 mg po, followed by 40 mg po qd with food
  - Available as a 40 and 80 mg capsule
  - $600/30 tablets ($700-840 per course)

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Betrixaban (Bevyxxa)

- Advantages
  - First orally administered anticoagulant demonstrated to be effective for VTE prophylaxis for in-hospital and extended-duration use in acutely ill medical patients
  - Is as effective or more effective than enoxaparin for VTE prophylaxis in acutely ill medical patients and is administered orally (vs. enoxaparin is SQ)
- Disadvantages
  - Labeled indications are more limited

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Agents for Atopic Dermatitis

- Most common form of eczema – chronic inflammatory skin disease
- Crisaborole (Eucrisa) – PDE inhibitor; topical preparation
  - May be more effective in some patients, less likely to cause systemic AE
  - Has not been directly compared to other drugs in clinical trials; limited indications; 60 grams $700
- Dupilumab (Dupixent) – human monoclonal antibody; SQ
  - Indicated for the treatment of adult patients with moderate to severe atopic dermatitis whose disease is not adequately controlled with topical preparations, or when topicals inadvisable.
  - Used with or without topical corticosteroids.
  - SQ 600 mg (two 300-mg injections at different sites); then 300 mg qoweek
  - $1700/300 mg

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Ocrelizumab (Ocrevus)

- Humanized monoclonal antibody indicated for treatment of patients with relapsing or primary progressive forms of multiple sclerosis
- Advantages
  - First drug shown to be effective in treatment of PPMS
  - More effective than interferon beta-1a in treatment of relapsing MS
  - Unique MOA (CD20-directed cytolytic antibody)
  - Administered less frequently (every 6 months vs. three times/week)
- Disadvantages
  - Administered IV in health care facility
  - Often causes infusion reaction; more likely to cause infection
  - May increase risk of malignancy

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Antiviral Agents for Hepatitis C

- More than 3 million Americans have chronic hepatitis C infection
  - At least six genotypes; 75% Americans have genotype 1
  - Direct-acting antiviral agents have high cure rates (> 90%)
- Harvoni – sofosbuvir and ledipasvir
- Zepatier – elbasvir and grazoprevir
- Epclusa – sofosbuvir and velpatasvir (first approved for all 6 genotypes)
- Technivie – ombitasvir and paritaprevir with ritonavir
- Viekira XR – dasabuvir, ombitasvir, paritaprevir with ritonavir

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Antiviral Agents for Hepatitis C

- Glecaprevir – pibrentasvir (Mavyret)
  - Highly effective for genotypes 1-6
  - 8 week treatment for most patients without cirrhosis and can be used with renal impairment (including those on dialysis)
  - SVR 95-100% of the patients in most studies
  - 8 week course ~ 12 week course (preferred for treatment-naïve patients with compensated cirrhosis)
  - Contraindicated in severe hepatic impairment; not recommended in moderate hepatic impairment
  - AE – headache (16%), fatigue (11%), nausea (9%), diarrhea (7%)

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Antiviral Agents for Hepatitis C

- Glecaprevir – pibrentasvir (Mavyret)
- Advantages (compared to sofosbuvir/velpatasvir)
  - Has been demonstrated to be effective in an 8-week course of treatment
  - Is effective in patients for whom certain previous HCV regimens have failed
  - Is not likely to interact with amiodarone and cause bradycardia
  - Effectiveness demonstrated in patients with severe renal impairment
- Disadvantages
  - Contraindicated in severe hepatic impairment, and not recommended in moderate
  - $16,000/4 weeks

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Antiviral Agents for Hepatitis C

- Volsevi - Sofosbuvir/velpatasvir/voxilaprevir
  - First product to be approved for patients who have been previously treated, but unsuccessfully, with certain other antiviral regimens for HCV infection
  - Indicated for adults with chronic HCV without cirrhosis, or with compensated cirrhosis, who have either:
    - Genotype 1, 2, 3, 4, 5, or 6 and previously treated with an HCV regimen containing an NS5A inhibitor, or
    - Genotype 1A or 3 infections and have been previously treated with an HCV regimen containing sofosbuvir without an NS5A inhibitor
  - Endpoint – sustained virologic response at 12 weeks after cessation of treatment – 96% vs. placebo

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Antiviral Agents for Hepatitis C

- Volsevi - Sofosbuvir/velpatasvir/voxilaprevir
  - AE – headache (21%), fatigue (17%), diarrhea (13%), nausea (13%)
  - Symptomatic bradycardia if concurrently taking amiodarone – may require pacemaker intervention; concurrent therapy not recommended
  - Systemic exposure of voxilaprevir is significantly increased if taken with food; combination should be taken with food
  - Numerous drug interactions
- Advantages – effective in patients for whom certain previous HCV regimens have failed
- Disadvantages – interacts with more medications; not recommended with moderate or severe hepatic impairment

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Plecanatide (Trulance)

- A 16 amino acid peptide indicated for the treatment of chronic idiopathic constipation in adults
  - Irritable bowel with constipation – early 2018 approval
- Similar to linaclotide (Linzess)
- MOA – guanylate cyclase-C (GC-C) agonist
  - Act locally on the luminal surface of the intestinal epithelium
  - Results in increased intestinal fluid and accelerated transit
- Effectiveness - 21% with plecanatide vs. 10-13% with placebo

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Plecanatide (Trulance)

- Contraindication and box warning about risk of serious dehydration in pediatric patients
  - Contraindicated in patients < 6 years of age; avoid 6-18 years of age
- Administer with or without food, swallow tablet whole (3 mg)
- AE – diarrhea (4-5% of patients)
- Advantages
  - May be administered without regard to food (linaclotide given on an empty stomach before first meal of the day)
- Disadvantages
  - Labeled indications in 2017 < linaclotide (but IBS-C approved in early 2018)
  - $424/month

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Naldemedine (Symproic) – a PAMORA

- Indicated for OIC in adult patients with chronic non-cancer pain, including patients with chronic pain related to prior cancer or its treatment who do not require frequent (e.g., weekly) opioid dosage escalation
- A derivative of naltrexone to which a side chain has been added, increasing the molecular weight and the polar surface area, and reducing its ability to cross the blood-brain barrier (BBB)
- Dose – 0.2 mg po once daily with or without food ($350/month)
- Drug interactions with 3A4 inducers/inhibitors, P-gp inhibitors

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Naldemedine (Symproic) – a PAMORA

- Clinical effectiveness
  - Responder – a patient who had at least 3 SBMs per week and a change from baseline of at least 1 SBM per week for at least 9 out of the 12 weeks and 3 out of the last 4 weeks in Studies 1 and 2
  - Study 1 – Naldemedine response 48%; placebo 35%
  - Study 2 – Naldemedine response 53%; placebo 34%
- DC naldemedine if opioid pain medication is discontinued

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COPD Inhalers

- Trelegy Ellipta - $575
  - Fluticasone furoate (corticosteroid)
  - Vilanterol (LABA)
  - Umeclidinium (LAMA)
- Glycopyrrolate
  - Seebri Neohaler (dry powder inhaler) - $475
  - Lonhala (glycopyrrolate inhalation solution) - TBA
    - For the long-term maintenance treatment of airflow obstruction in patients with COPD
    - First nebulized LAMA approved for COPD, and first use of Magnair, closed eFlow technology system

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Diabetes

- Fiasp – insulin aspart injection, formulated with niacinamide to help increase speed of initial insulin absorption
  - Appears in circulation 2.5 minutes after administration
  - Maximum insulin concentration achieved in about 63 minutes after administration
  - In T1DM – non-inferior to NovoLog (both in combination with Detemir)
  - In T2DM – non-inferior to NovoLog (both in combination with metformin)
- Admelog – insulin lispro injection
  - Approved as SQ injection, SQ infusion (insulin pump) or IV infusion

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Diabetes

- Ertugliflozin (Steglatro)
  - Sodium-glucose co-transporter 2 (SGLT2) inhibitor
- Ertugliflozin and sitagliptin (Steglujan) – both in T2DM
  - Sitagliptin is a dipeptidyl peptidase-4 (DPP-4) inhibitor
- Semaglutide injection
  - GLP-1 receptor agonist

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First OTC Low-Dose Brimonidine Eye Drop

- Approved for ocular redness
- Lumify 0.025% - brimonidine tartrate ophthalmic solution
- A selective alpha-2 adrenergic receptor agonist, works by selectively constricting the veins in the eye, increasing the availability of oxygen to surrounding tissue and reducing the likelihood of rebound redness
  - 95% improvement at 1 minute
  - Reduced redness for up to 8 hours

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Once-Monthly Buprenorphine

- FDA approved Sublocade, a once-monthly buprenorphine injection for moderate to severe opioid use disorder
- Current option of buprenorphine is dissolvable film or tablets taken daily, or implant (Probuphine)
- Sublocade allows sustained delivery of buprenorphine over a one month period
  - On SQ injection, it forms a solid depot, subsequently broken down steadily release the drug
  - Dose is delivered by a prefilled syringe by a clinician

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Shingrix (Zoster Vaccine Recombinant)

- Indicated for prevention of herpes zoster (shingles) in adults aged 50 years and older
  - Not indicated for prevention of primary varicella infection (chickenpox)
  - Intramuscular injection
- Dosing schedule
  - Two doses (0.5 mL each) administered IM as follows:
    - First dose at Month 0
    - Followed by a second dose administered anytime between 2 and 6 months later

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CDC Recommendations - Shingrix

- CDC advises Shingrix be given to people starting at age 50, a full 10 years earlier than its advice for Zostavax
- CDC recommends those who received Zostavax should now get Shingrix as well; Shingrix is the preferred vaccine over Zostavax
- Those who have had shingles should also receive Shingrix
- Shingrix thought to provide substantially long, persistent protection
  - Contains adjuvant to boost effect
- AE – pain at injection site, redness and swelling, muscle pain, immune system responses such as headache, shivering, fever, and upset stomach
- $280 for two shot series

https://www.consumerreports.org/shingles-vaccine/new-shingles-vaccine-shingrix-what-you-should-know/

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Buh-bye! Opana ER pulled from market

- FDA requested the removal of Opana ER (oxymorphone HCl extended-release tablets) from the market
- Endo voluntarily complied
- After a review of postmarketing data showed a significant shift in the route of abuse from nasal to injection after the drug was reformulated
- The abuse of reformulated Opana ER via injection had been linked to a serious outbreak of HIV and hepatitis C infections, and thrombotic microangiopathy

https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm562401.htm

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Cough and Cold Medicines

- Cough and cold medicines containing codeine and hydrocodone now limited to adults ≥ 18 years old
- Also added new safety information regarding the risks of slowed or difficult breathing, misuse, abuse, addiction, overdose and death to the boxed warning
- Due to risk analysis – risk of slowed or difficult breathing, misuse, abuse, addiction, overdose, and death with these medications outweighed their benefit in patients < 18 years of age
- Consider dextromethorphan or benzonatate instead

https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm592109.htm

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Codeine and Tramadol
(now there's a pair to beat a full house)

- FDA reminds healthcare professionals that tramadol and single-ingredient codeine meds are only approved for adult use
- FDA also recommends against use by breastfeeding mothers as well
- Labeling changes:
  - Contraindication – codeine for pain or cough, or tramadol for pain in children < 12 years of age
  - Contraindication – tramadol in children < 18 years of age after surgery to remove tonsils and/or adenoids
  - Warning – codeine and tramadol in adolescents 12-18 years who are obese or have OSA or severe lung disease
  - Strengthened warning about breastfeeding

https://www.fda.gov/Drugs/DrugSafety/ucm549679.htm

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IBS Drug Linked to Pancreatitis

- FDA warning that eluxadoline (Viberzi) should not be used in patients without a gallbladder due to an increased risk of developing serious pancreatitis that could lead to hospitalization or death
- Eluxadoline is a mu-opioid agonist approved to treat IBS-D
- Since approval (Mary 2015) through February 2017, FDA received 120 reports of serious cases of pancreatitis or death (ok, when is death not serious?)
  - Of the 68 patients who provided gallbladder status, 56 were MIA
- Do not use eluxadoline in patients with no gallbladder, gallbladder blockage or sphincter of Oddi problem, pancreatitis, serious liver problems, chronic or severe constipation, intestinal obstruction, alcohol abuse, alcohol addiction, drinks > 3 alcoholic beverages/day

https://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm546771.htm

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FDA Approves L-glutamine for Sickle Cell

- L-glutamine oral powder (Endari) for oral administration to reduce the acute complications of sickle cell disease in adult and pediatric patients 5 years or older
- Clinical trial
  - 230 patients (age 5-58) with sickle cell anemia or sickle thalassemia with 2 or more painful crises within previous 12 months
  - Randomized to either L-glutamine or placebo for 48 weeks
  - L-glutamine group – 3 sickle cell crises vs. 4 with placebo
  - AE – constipation, nausea, headache, abdominal pain, cough, pain in extremity, back and chest pain
- Dose – 10 grams to 30 grams per day (based on weight), po, BID

https://www.fda.gov/Drugs/InformationOnDrugs/ApprovedDrugs/ucm566097.htm

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Zilretta for OA of Knees Pain

- Triamcinolone acetonide extended-release injectable suspension
- Intra-articular – first XR injection for OA knee pain
- Triamcinolone acetonide is a short-acting corticosteroid, with a poly lactic-co-glycolic acid matrix to provide pain relief over 12 weeks
- Compared to a single intra-articular injection or immediate release TCA 40 mg, Zilretta showed 50% reduction in pain from baseline through week 12.

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New Dosage Formulations

Brand	Generic	Description
Abilify MyCite	Aripiprazole plus sensor	New drug-device combination product with tablets embedded with a tracking sensor to ensure ingestion
Lyrica CR	Pregabalin	New extended-release tablets for diabetic peripheral neuropathy and postherpetic neuralgia
Arymo ER	Morphine	New extended-release tablet for severe pain
Carospir	Spironolactone	New oral suspension formulation aldosterone antagonist diuretic
Cotempla XR-ODT	Methylphenidate	New extended-release orally disintegrating tablet formulation for AHDH
Roxybond	Oxycodone	New opioid analgesic formulation for management of severe pain
Vantrela ER	Hydrocodone	New extended-release tablets for severe pain

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Antimicrobials

Generic	Brand	Indication/Comment
Letermovir	Prevymis	Cytomegalovirus prophylaxis in allogeneic hematopoietic cell transplant recipients
Secnidazole	Solosec	Bacterial vaginosis
Benznidazole		Chagas disease (infection with *Trypanosoma cruzi,* parasitic infection)
Glecaprevir-pibrentasvir and sofosbuvir-velpatasvir-voxilaprevir	Mavyret Vosevi	Chronic Hepatis C
Delafloxacin	Basdela	Treatment of skin and soft tissue infections
Raltegravir	Isentress	New once-daily formulation integrase strand transfer inhibitor for treatment-naïve HIV patients

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Hematologic/Chemotherapeutic

Brand	Generic	Description
Aliqopa	Copanlisib	A kinase inhibitor for relapsed follicular lymphoma
Alunbrig	Brigatinib	A kinase inhibitor for a certain type of non-small cell lung cancer
Calquenbce	Acalabrutinib	A kinase inhibitor for mantle cell carcinoma
Idhifa	Enasidenib	An oral isocitrate dehydrogenase-2 inhibitor for acute myeloid leukemia
Kisqali	Ribociclib	A kinase inhibitor for postmenopausal women with advanced breast cancer
Nerlynx	Neratinib	An oral kinase inhibitor extended adjuvant therapy for breast cancer
Rydapt	Midostaurin	A kinase inhibitor for patients with acute myeloid leukemia (AML) and other rare blood disorders
Verzenio	Abemaciclib	A kinase inhibitor for advanced breast cancer
Zejula	Niraparib	A PARP inhibitor for recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer

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Crazy Drugs in the Pipeline

- FDA just granted a breakthrough therapy designation to MDMA
  - Ecstasy – midomafetamine
  - For post-traumatic stress disorder
  - In phase 2 trials with 107 patients, after three sessions of MDMA-assisted psychotherapy, 61% of patients no longer had symptoms to PTSD
- RP-G28 – treatment of lactose intolerance
  - Lactose intolerance affects one billion people worldwide!
  - Stimulated growth of lactose-metabolizing bacteria in the colon, reduces gas production, which in turn relieves the symptoms of lactose intolerance

http://drugtopics.modernmedicine.com/drug-topics/news/top-7-craziest-drugs-pipeline

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Crazy Drugs in the Pipeline

- Biotin (Vitamin B_7) – now in phase 3 trials for the treatment of progressive MS
  - In one pilot study of 23 patients, 21 patients (91.3%) improved clinically
- Epidiolex – an oral solution of pure plant-derived cannabidiol
  - Current in several Phase 3 trials for multiple indications
    - Dravet syndrome, Lannon-Gastaut syndrome, Tuberous Sclerosis Complex, Infantile Spasms
  - FDA has granted expanded access to Epidiolex, allowing physicians to apply for emergency access to the drug for patients suffering from intractable epilepsy

http://drugtopics.modernmedicine.com/drug-topics/news/top-7-craziest-drugs-pipeline

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Questions?

http://drugtopics.modernmedicine.com/drug-topics/news/top-7-craziest-drugs-pipeline

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Exam Questions:

1. Which of the following would be an example of a tyramine-containing food, that patients taking safinamide should avoid?
    a. Aged cheese
    b. Grapefruit juice
    c. Potato chips
    d. Chocolate

2. Valbenazine (Ingrezza) is used to treat which of the following indications?
    a. Orthostatic hypotension with Parkinson's disease
    b. Diabetes mellitus
    c. Atopic dermatitis
    d. Tardive dyskinesias

3. What is the difference between deutetrabenazine and tetrabenazine?
    a. Deutetrabenazine causes more adverse effects
    b. Tetrabenazine is substantially more effective
    c. Duetetrabenazine is dosed twice a day instead of three times a day
    d. The deutetrabenazine is far more cost-effective

4. Bezlotoxumab (Zinplava) is used to treat which of the following conditions?
    a. Recurrence of *C. difficile* infection
    b. Complicated gram-negative urinary tract infections
    c. Atopic dermatitis
    d. Relapsing-remitting multiple sclerosis

5. Dupilumab (Dupixent) is used for which of the following indications?
    a. Prophylaxis of VTE during and after acute hospitalization
    b. Moderate to severe atopic dermatitis
    c. Chorea associated with Huntington's disease
    d. Post-operative pain

6. Ocrelizumab is the first medication used to treat THIS indication?
    a. Relapsing-remitting multiple sclerosis
    b. Primary progressive multiple sclerosis
    c. Huntington's chorea
    d. Amotrophic lateral sclerosis

7. Plecanatide (Trulance) acts locally on the luminal surface of the intestinal epithelium to increase intestinal fluid and accelerated transmit, similar to which of the following medications?
    a. Lubiprostone
    b. Methylnaltrexone
    c. Linaclotide
    d. Bisacodyl

8. Naldemedine is a PAMORA that doesn't cross the blood barrier, through which of the following mechanisms?
    a. The methyl group makes it a quaternary ammonium
    b. The pegylated chain attached to the molecule
    c. It's a zwitterion (zwitterions rule!)
    d. It's a derivative of naltrexone with a side chain that increases molecular weight and polarity

9. Brimonidine has been approved as an over-the-counter product for which indication?
    a. Ocular redness
    b. Ocular itching
    c. Ocular weeping
    d. Ocular discharge

10. Why has the CDC recommended patients receive Shingrix instead of Zostavax?
    a. Greater immunity in 50's, 60's, 70's and 80's
    b. Greater efficacy
    c. Less risk post-herpetic neuralgia
    d. All of the above!