

# Drug Updates for 2017

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# Objectives

1. Name the new pharmaceutical agents available for clinical practice.
2. Explain the use of new pharmaceutical agents in clinical practice.
3. Summarize the benefits, risks, and alternatives of new pharmaceutical agents.

# 2017 Was A Busy Year

- FDA approved 23 new drugs and biologics which is up from a sluggish 22 in 2016
- The 11 year average is 25 novel new drugs per year
- 2017 stands out because many of these new drugs were one of a kinds or first in class
- Reflects a trend to create drugs that focus specific cancers and rare diseases
- But there was also growth for primary care .....

# Endocrine



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# Semaglutide (Ozempic)

- GLP-1 analog
- Indication:
  - Type 2 DM
- Dose:
  - 0.25mg once weekly SC injection x 4 weeks then 0.5mg/week x 4 weeks then if needed max of 1mg/week
- Efficacy:
  - On average BS was lowered 2 ½ times more than DPP-4
  - Weight loss was noted to be 2-3x more vs. comparison group.
- Safety: Increased amylase and lipase, N/V
- Cost:
  - \$676

# Dapagliflozin/Saxagliptin (Qtern)

- Combining SGLT2 inhibitor with DPP-4 inhibitor
- Indication:
  - Management of DM2
- Dose:
  - Dapagliflozin 10mg/Saxagliptin 5mg daily
- Efficacy: Additive efficacy of two classes
- Safety:
  - Hypoglycemia, weight gain
- Cost:
  - \$490/month

# Neurology



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# AES Question

To be placed prior to a Poll Question. Duplicate as needed.



<https://commons.wikimedia.org/wiki/File:Circle-question-blue.svg#/media/File:Circle-question-blue.svg>



Which medication has a black box warning outlining use should not exceed 12 weeks secondary to increasing risk of developing tardive dyskinesia?

- A. Aripiprazole (Abilify)
- B. Mirtazapine (Remeron)
- C. Quetiapine (Seroquel)
- D. Metoclopramide (Reglan)

# Valbenazine (Ingrezza)

- Vesicular Monoamine Transporter 2 Inhibitor (VMAT2) and Central Monoamine-Depleting Agent
- Indication:
  - Tardive Dyskinesia
  - MOA is unknown but it looks to reduce synaptic monoamine concentrations
- Dose:
  - Initial 40mg daily x 1 week then 80mg daily
- Efficacy:
  - Placebo controlled trial showed AIMS scored improved on active medication
  - Placebo group re-randomized and once again improvement noted on movements
- Safety:
  - Somnolence, QT prolongation, and no use in suicidal or violent patients
  - Does undergo metabolism with CYP 3A4/5 and 2D6
- Cost:
  - \$6330/month

# Vascular



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# Betrixaban (Bevyxxa)

- Factor Xa inhibitor
- Indication:
  - Extended-duration prophylaxis of VTE in hospitalized patients who are high risk for VTE
- Dose:
  - 160mg x 1 then 80mg daily with food x 35 to 42 days
  - CrCl  $\geq 15$  and  $\leq 30$ ml/min use 80mg x 1 and then 40mg daily
- Efficacy:
  - APEX study showed non-inferior to enoxaparin
- Safety:
  - Risk of minor bleeding events is slightly higher (3.1% vs 1.6%)
  - Incidence rate for all bleeding episodes was 2.4% vs 1.2% for enoxaparin
  - Overall fewer ADRs vs LMWH - major bleeding risk was similar (0.67% vs 0.57%)
- Cost:
  - Approximately \$600/month

# Infectious Disease



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# Delafloxacin (Baxdela)

- First Fluoroquinolone antibiotic with activity against MRSA
- Indication:
  - Acute bacterial skin and skin structure infections and covers Gram (-) ESBL bacteria
- Dose:
  - IV: 300mg q 12 h
  - Oral: 450mg q 12h up to 14 days
  - Dose adjust IV if CrCl <30ml/min and cannot use either dosage form if CrCL <15ml/min
- Efficacy:
  - Noninferior to vancomycin + aztreonam
  - Clinical response seen within 72h
- Safety:
  - GI most common and does carry class boxed warnings EXCEPT
  - No QT prolongation or photosensitivity
  - If SCr increases on IV switch to PO
- Cost:
  - \$1620/10d course

# Secnidazole (Solosec)

- Nitroimidazole antibiotic that interferes with DNA synthesis of bacteria
- Indication:
  - Single dose treatment of bacterial vaginosis
- Dose:
  - 2g x 1 dose
  - Sprinkle on applesauce, yogurt, or pudding and eat within 30 minutes
  - Breastfeeding should be stopped for 96h post dose
- Efficacy:
  - Two clinical trials show cure rates within 21-30d post treatment of 53% and 68% vs 19% and 18% with placebo
- Safety:
  - Candidiasis, HA, GI
- Cost:
  - Not published yet

# Sofosbuvir/Velpatasvir/Voxilaprevir (Vosevi)

- Fixed dose combination of NS5B RNA polymerase inhibitor + NS5A replication complex inhibitor + NS3/4 Protease Inhibitor
- Indication:
  - Salvage treatment or retreatment
    - Genotypes 1-6 without cirrhosis or with compensated liver previously using an NSA5A inhibitor
    - Genotypes 1a or 3 previously treated with regimen containing sofosbuvir without an NSA5A inhibitor
- Dose:
  - 1 fixed dose tablet daily x 12 weeks
- Efficacy:
  - POLARIS-1 trial showed sustained virologic response (SVR) ~95%
- Drug Interactions:
  - Statins, Digoxin, Dabigatran, Ethinyl estradiol, and Amiodarone
- Safety:
  - HA, fatigue, GI, insomnia, reactivation of HBV infections
- Cost:
  - Month supply cost \$30,000 x 3 months= \$90,000



# Glecaprevir/Pibrentasvir (Mavyret)

- Fixed dose combination of NS5A replication complex inhibitor + NS3/4A PI
- Indication:
  - Genotypes 1-6 without cirrhosis or compensated cirrhosis
  - Therapy ranges 8-16 wks based on genotype and previous therapies s
- Dose:
  - Treatment-naïve 3 tablets daily x 8 weeks
- Efficacy:
  - ENDURANCE and SURVEYOR trials showed SVR 95 to 99% depending on the genotype
  - SVR was seen at 8 weeks and was not greater at 12 weeks
- Drug Interactions:
  - Statins, Digoxin, Dabigatran, Ethinyl estradiol, and Amiodarone
- Safety:
  - Fatigue, HA, GI
- Dosage Form:
  - \$26,400 for entire 8 week course

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# Shingrix is what type of vaccine?

- A. Recombinant
- B. Live
- C. Conjugated
- D. None of the above

# Zoster Vaccine (Shingrix)

- Recombinant vaccine
- Indication:
  - Prevention of herpes zoster in those  $\geq 50$ yo
- Dose:
  - 50 mcg given as 2 dose series (0 then 2-6mos)
- Efficacy:
  - 97% vs 51% over three years
  - Zostavax: NNT ~ 59 patients to prevent 1 case of shingles over 3 years in pts > 60yo
  - Shingrix: NNT ~ 37 patients to prevent 1 case of shingles over 3 years in pts at least 50yo
  - Shingrix: expected to have 90% efficacy at least 4 years post vaccination in all ages
  - Shingrix: expected  $\geq 60$ yo that there will be 10 cases after 4 years vs 105 cases with Zostavax
- Safety:
  - >10%: Fatigue, HA, shivering/fever, myalgia, GI effects, injection site pain
- Cost:
  - \$150 per dose

# Bone and Joint



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# Lesinurad/Allopurinol (Duzallo)

- First combination of URAT1 inhibitor with xanthine oxidase inhibitor
- Indication:
  - Chronic management of hyperuricemia associated with gout
- Dose:
  - Lesinurad 200mg/Allopurinol 200mg or 300mg/d
- Efficacy:
  - CLEAR 1, CLEAR 2 and CRYSTAL trials all showed lower UA levels ( $\leq 6$ mg/dl) after a year with combination therapy vs monotherapy
  - Mean gout flare rates were not effected per CLEAR trials
  - Non-inferior to the two medications used separately
- Safety:
  - HA, heartburn
  - Did have an increase in SCr at higher doses
  - Black Box warning: possible that it may cause ARF at higher doses
- Cost:
  - \$450/month same as Lesinurad alone

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It is recommended that bisphosphonates be used concomitantly with parathyroid-related analogs to manage osteoporosis.

A. True

B. False



# Abaloparatide (Tymlos)

- Human parathyroid hormone related analog
- Indications:
  - Treatment of postmenopausal women with osteoporosis at high fracture risk
  - Use up to 2 years
- Dose:
  - 80mcg SC daily
- Efficacy:
  - ACTIVE trial and ACTIVEExtend trial-consistent significant and rapid reductions in the risk vertebral and nonvertebral fx
  - ACTIVE trial RRR 86% in new vertebral fractures and 43% in nonvertebral fx with ARR of 3.6% and 2.0%, respectively.
- Safety:
  - Increased uric acid, hypercalcemia, injection site reaction, Dz, HA, GI
  - Black Box warning: increase in the incidence of osteosarcoma
- Cost:
  - Approximately \$1950/month vs. Forteo at \$3500/month

# Gastrointestinal Health



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Which side effect caused by opioids does not lessen as tolerance increases?

- A. Respiratory depression
- B. Itching
- C. Constipation
- D. Somnolence

# Naldemedine (Symproic)

- Selective opioid antagonist at peripheral mu receptors in GI tract, does not cross the BBB
- Indication:
  - Opioid induced constipation chronic non-cancer pain
- Dose:
  - 0.2mg/day taken with or without food and no renal dose adjustment needed
- Efficacy:
  - 3 trials with over 2000 pts
  - Third trial allowed patients to continue other constipation meds and ran for 52 weeks
  - Increase in spontaneous bowel movements to at least 3 bowel/week vs placebo.
- Adverse Effects:
  - Withdrawal like symptoms: abdominal pain, flatulence, N/V, dz, sweating, anxiety, chills
  - Possible increase in perforation in those with h/o PUD, GI cancers, or diverticular disease
  - Strong CYP 3A4 impact so watch interactions
- Cost:
  - \$330/month vs. \$650 for Relistor

# Plecanatide (Trulance)

- Guanylate Cyclase-c agonist leading to increased fluid secretion in intestine
- Indication:
  - Chronic idiopathic constipation
- Dose:
  - 3mg/day taken with or without food and no renal dose adjustment needed
- Efficacy:
  - 2 trials with over 1700 pts over 12 weeks
  - Increase in spontaneous bowel movements to at least 3 bowel/week vs placebo.
- Adverse Effects:
  - Diarrhea, abdominal distention, flatulence with little systemic absorption
- Cost:
  - \$424/month

# Biologics



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# Biosimilar Expansion in 2017

- Highly similar to FDA approved biologics in physiochemical characteristics, purity, potency, efficacy and safety
- Three approved in 2016:
  - ***Adalimumab-ADBM (Cyltezo) and Adalimumab-atto (Amjevita) – Similar to Humira***
    - *Indications vary based on product eg. Crohn's, UC, RA, anklyosing spondylitis, psoriasiss*
  - ***Infliximab-ABDA (Renflexis) and Infliximab-dyyb (Inflectra) – Similar to Remicade***
    - *Indications vary based on product eg. Crohn's, RA, ankylosing spondylitis, psoriasis*
- Substitution or Interchange of products
  - BPCI Act of 2009 gives 1 yr of exclusive marketing rights to the first biosimilar approved
  - These two are beyond their year so more biosimilars in 2017.
  - Can be done without prescriber input but watch indications they vary
- Naming is based on a random 4 letter suffix devoid of meaning
  - Allows differentiation of biosimilars with suffix evening playing field
  - Common core names group them within EMR



Did Not Make the Show



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# Approved in 2017

- Airduo Resplick - ICS/LABA
- Armonair Resplick - ICS
- Lyrica CR - extended release for PN
- Bydureon Bcise - GLP 1 in new pen
- Kedrab – Rabies IG
- Oactra – House dust miter extract
- Minolira - ER minocycline
- Niktia and Zypitamag - new salts of Pitavastatin
- Jadenu Sprinkles - granules
- Opana ER - PULLED from market

# Best Practice Recommendations

- Evolution of industry showing research in areas that will yield high profits ie biologics, DM care, autoimmune diseases
- Primary Care physicians on average usually wait 12-18 months to use a new product.
- Awareness is crucial to determine when and in what type of patient a new product may work
- Quick and easy information is needed for the current pace of life
- Choose three resources that fit your needs
  - Prescribers Letter
  - Lexicomp App
  - Medscape
  - AAFP daily emails
  - <https://www.fda.gov/Drugs/InformationOnDrugs/ucm412998.htm>
  - <https://www.centerwatch.com/drug-information/fda-approved-drugs/>
  - Others?!

# Answers

- D
- A
- B
- C



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