Drug Update 2018: What's New?

Wendy L. Wright,
MS, ANP-BC, FNP-BC, FAANP, FAAN, FNAP
Owner & President:
Wright & Associates Family Healthcare, Amherst
Wright & Associates Family Healthcare, Concord
Owner – Partners in Healthcare Education, LLC

Disclosures

- Speaker Bureau: Sanofi-Pasteur, Merck, Abbott, Pfizer
- Consultant: Sanofi-Pasteur, Pfizer, Arbor, Merck

Objectives

- Upon completion of this learning activity, the participant will be able to:
  - Identify 5 – 10 new medications
  - Discuss the use, side effects, drug-drug interactions, and benefits of each of the medications
  - Discuss updates related to labeling, indications, risks associated with various medications

New Drugs

2017: What Happened?

U.S. FDA approved novel 46 medications in 2017
Average: 28 between 2006 – 2014
Only 8 medications for primary care

https://www.fda.gov/Drugs/DevelopmentApprovalProcess/DrugInnovation/ucm537040.htm accessed 12-28-2017

Endocrinology

Semaglutide (Ozempic)

- Class: GLP-1 receptor agonist
- Indication: Adjunct to diet and exercise in adults with Type 2 diabetes
- Dosage:
  - Start at 0.25 mg once weekly; if tolerating well – advance to 0.5 mg after 4 weeks (subcutaneous injection)
  - If additional glycemic control is needed, after 4 weeks – advance to 1 mg once weekly
  - Can be taken any time of the day
  - No relationship to meals is required

https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/209637lbl.pdf accessed 12-28-2017

Semaglutide

- Warnings and Precautions:
  - Pancreatitis (as with other agents in the class)
  - Hypoglycemia (when combined with sulfonylureas or basal insulins)
  - Avoid in pregnancy and lactation
    - Discontinue 2 months before pregnancy is planned due to long washout period
- Contraindications:
  - Personal or family history of medullary thyroid carcinoma or patients with multiple endocrine neoplasia syndrome

https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/209637lbl.pdf accessed 12-28-2017

Semaglutide

- 3150 patients exposed to drug (7 trials)
- Compared to (statistically significant):
  - Sitagliptin
  - Once weekly exenatide
  - Placebo
- A1C: decreased by 1.2%; 73% achieved A1C < 7.0% from placebo
- Fasting glucose: decreased by 41 mg/dL

https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/209637lbl.pdf accessed 12-28-2017

Semaglutide

- Side effects (0.5 mg and 1mg):
  - Nausea (15.8% (20.3%) vs. 6.1% placebo)
  - Vomiting (5% (9.2%) vs. 2.3% placebo)
  - Diarrhea (8.5% (8.8%) vs. 1.9% placebo)
  - Abdominal pain (7.3% (5.7%) vs. 4.6% placebo)
  - Constipation (5.0% (3.1%) vs. 1.5% placebo)

https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/209637lbl.pdf accessed 12-28-2017

Semaglutide

- Drug – Drug Interactions
  - Delays gastric emptying
- Advantages
  - Another GLP-1 receptor agonist
  - Studied in individuals 75 years and older without any increase in adverse events
  - No dosage adjustment in patients with liver or kidney disease
- Disadvantages
  - Concern re: worsening retinopathy
  - If patients have retinopathy, they should be monitored regularly

https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/209637lbl.pdf accessed 12-28-2017

Ertugliflozin (Steglatro)

- Class: SGLT2 inhibitor
- Indication: Adjunct to diet and exercise in adults with Type 2 diabetes
- Dosage:
  - 5 mg once daily in the morning
  - Take with or without food
  - Maximum dosage: 15 mg once daily

https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/209803s000lbl.pdf accessed 12-28-2017

Ertugliflozin

- Precautions and Contraindications
  - Do not use in patients with an estimated glomerular filtration rate (eGFR) below 30 mL/minute
  - Initiation is not recommended in patients with an eGFR of 30 to less than 60 mL/minute
  - Continued use is not recommended in patients with an eGFR persistently between 30 and less than 60 mL/min
  - Do not use in pregnancy and lactation

https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/209803s000lbl.pdf accessed 12-28-2017

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Ertugliflozin

- Precautions and Contraindications
  - Urosepsis and Pyelonephritis: Evaluate patients for signs and symptoms of urinary tract infections and treat promptly, if indicated
  - Lower Limb Amputation: Before initiating, consider factors that may increase risk of amputation. Monitor patients for infections or ulcers of lower limbs, and discontinue if these occur
  - Genital Mycotic Infections: Monitor and treat if indicated

https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/209803s000lbl.pdf accessed 12-28-2017

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Ertugliflozin

- 1029 patients (two trials)
- A1C:
  - Decreased by 0.7% (5 mg) and 0.9% (15 mg)
  - 36.3% and 43.3% (5 mg and 15 mg respectively) achieved A1C < 7.0% compared to placebo placebo
- Fasting glucose: decreased by 30.3 mg/dL (5 mg) and 40.9 mg/dL (15mg)

https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/209803s000lbl.pdf accessed 12-28-2017

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Ertugliflozin

- Side effects:
  - Female genital mycotic infections 9.1% vs. 3.0% placebo)
  - Male genital mycotic infections 3.7% vs. 0.4% placebo)
  - Urinary tract infections (4.0% vs. .39% placebo)
  - Headache (3.5% vs. 2.3% placebo)
  - Vaginal pruritus (2.8% vs. 0.4% placebo)

https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/209803s000lbl.pdf accessed 12-28-2017

Ertugliflozin

- Monitor:
  - Watch blood pressure, particularly in those $\geq$ 65 years and/or with impaired renal function (concern regarding volume depletion)
  - Class: Increased LDL and increased hemoglobin
- Drug – Drug Interactions
  - No significant d-d interaction
  - Caution hypoglycemia when added to other medications

https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/209803s000lbl.pdf accessed 12-28-2017

Ertugliflozin

- Advantages
  - Another SGLT2 inhibitor

https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/209803s000lbl.pdf accessed 12-28-2017

New Insulins

- Insulin aspart (Fiasp)
  - Indication: Adults with Type 1 and Type 2 diabetes
  - Rapid acting insulin
  - Prefilled pen
- Insulin lispro (Humalog Junior KwikPen)
  - Indication: Type 1 and Type 2 diabetes
  - Rapid acting insulin
  - Half-unit pen

www.eMPR.com/news accessed 12-29-2017

Respiratory

Benralizumab (Fasenra)

- Indication:
  - Patients 12 years and older with severe asthma and the eosinophilic phenotype
- Class:
  - Interleukin-5 antagonist monoclonal antibody
    - Reduces eosinophil production and eosinophil survival
  - Add on to other medications indicated for asthma

https://www.azpicentral.com/fasenra/fasenra_pi.pdf accessed 12-28-2017

Benralizumab

- Dosage:
  - 30 mg SC every 4 weeks for the first three doses
  - Then….every 8 weeks
  - Recommended to be administered by HCP
- Warnings and precautions
  - Caution in pregnancy and lactation
    - No human data available
  - Anaphylaxis
- Contraindications:
  - Status asthmaticus or acute asthma

https://www.azpicentral.com/fasenra/fasenra_pi.pdf accessed 12-28-2017

Benralizumab

- Efficacy:
  - 52 week clinical trial with 609 patients
  - Reductions in: exacerbations, exacerbations requiring hospitalizations, reductions in ER visits, time to first exacerbations, and improvement in FEV1
- Drug – Drug Interactions
  - No significant drug-drug interactions

https://www.azpicentral.com/fasenra/fasenra_pi.pdf accessed 12-28-2017

Benralizumab

- Side effects
  - Headache (8% vs. 6%)
  - Pharyngitis (5% vs. 3%)
  - Fever (3% vs. 2%)
- Advantages
  - Another option for patients with severe asthma
- Disadvantages
  - Cost

https://www.azpicentral.com/fasenra/fasenra_pi.pdf accessed 12-28-2017

Benralizumab

- Competition:
  - Direct competitors
    - Reslizumab (Cinqair)
    - Mepolizumab (Nucala)
  - Different product/profile (Omalizumab – Xolair)

https://www.azpicentral.com/fasenra/fasenra_pi.pdf accessed 12-28-2017

Women's Health

Secnidazole (Solosec)

- Class:
  - Nitroimidazole antimicrobial
- Indication:
  - Treatment of bacterial vaginosis in adult women
- Dosage:
  - Single 2-gram packet of granules once orally
  - Sprinkle the packet onto applesauce, yogurt or pudding
  - Consume within 30 minutes without chewing or crunching the granules
  - Okay to drink water after ingesting the medication

https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/209363s000lbl.pdf Accessed 12-28-2017

Secnidazole

- Warnings and Precautions:
  - Carcinogenicity has been seen in mice and rats treated chronically with nitroimidazole derivatives
    - It is unclear if there is the same risk to patients taking a single dose to treat bacterial vaginosis
    - Avoid chronic use of this product
  - Avoid in pregnancy or lactation
    - No breastfeeding for 96 hours after the dosage
- Drug-drug interactions: None

https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/209363s000lbl.pdf
Accessed 12-28-2017

Secnidazole

- Efficacy (Two trials)
  - Responders:
    - 67.7% vs. 17.7%
    - 57.9% vs. 24.6%
- Side effects:
  - Vulvovaginal candidiasis (9.6% vs. 2.9%)
  - Headache (3.6% vs. 1.5%)
  - Nausea (3.6% vs. 0.7%)
  - Diarrhea (2.5% vs. 0.7%)

https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/209363s000lbl.pdf
Accessed 12-28-2017

Secnidazole

- Advantages
  - Another option to metronidazole
  - Single dose has equal efficacy to bid metronidazole for 2 - 7 days
  - No alcohol warning
  - Well-tolerated
- Disadvantages
  - Cost not yet available (first quarter of 2018)

https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/209363s000lbl.pdf
Accessed 12-28-2017

Abaloparatide (Tymlos)

- Class:
  - a human parathyroid hormone related peptide analog
- Indication:
  - Treatment of postmenopausal women with osteoporosis at high risk for fracture
- Dosage:
  - 80 mcg subcutaneously once daily
  - subcutaneous injection into periumbilical region of abdomen

https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/208743lbl.pdf accessed 12-28-2017

Abaloparatide

- Warnings and Precautions
  - Instruct patients to lie down during administration due to reports of orthostatic symptoms (for first few doses)
  - Avoid in patients with hypercalcemia
  - Osteosarcoma (rats/mice): class label
  - Not recommended in individuals with Paget's disease
  - Limit use to 2 years

https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/208743lbl.pdf accessed 12-28-2017

Abaloparatide

- Efficacy:
  - 1139 patients exposed to medication over 18 – 25 months
  - Increased BMD (8.8% vertebral spine, 3.5% hip)
  - Significant reduction in new vertebral fractures (0.6% compared to 4.2% placebo, $p < 0.0001$) and non-vertebral fractures
- Drug – drug interactions: NONE
- Competition:
  - Teriparatide (Forteo)

https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/208743lbl.pdf accessed 12-28-2017

Abaloparatide

- Side effects
  - Hypercalciuria (11% vs. 9%)
  - Dizziness (10% vs. 6%)
  - Nausea (8% vs. 3%)
  - Headache (8% vs. 6%)
  - Injection site reactions (58% vs. 28%)
- Lab changes:
  - Increase in calcium
  - Increase in uric acid

https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/208743lbl.pdf accessed 12-28-2017

Abaloparatide

- Advantages:
  - No dosage adjustment for mild – severe renal disease
- Disadvantages:
  - Cost (approximately $1600.00 per month)
  - Subcutaneous injection
  - Store in refrigerator

https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/208743lbl.pdf accessed 12-28-2017

Gastroenterology

Naldemedine (Symproic)

- Class:
  - Opioid antagonist
  - Peripherally acting mu opioid receptor antagonist in the GI tract
- Indication:
  - Treatment of opioid induced constipation (OIC) in adult patients with chronic non-cancer pain
- Dosage:
  - 0.2 mg once daily with or without food

https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/208854s000lbl.pdf
Accessed 12-29-2017

Naldemedine

- Warnings and Precautions:
  - Monitor for opioid withdrawal
  - Monitor for abdominal pain
- Contraindications:
  - Known or suspected GI obstruction
  - Avoid in patients with severe liver disease, pregnant or lactating

https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/208854s000lbl.pdf
Accessed 12-29-2017

Naldemedine

- Efficacy:
  - 12 week efficacy trials
  - More than 1000 patients enrolled in trials
  - 48% of patients on drug responded (35% placebo)
    - Responder: $\geq$ 3 SBMs per week and a change from baseline of $\geq$ 1 SBM/week for 9 of 12 weeks
    - Overall: approximately 2.3 – 3.3 more SBM's per week compared with placebo which was 1.5 – 2.3

https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/208854s000lbl.pdf
Accessed 12-29-2017

Naldemedine

- Side effects:
  - Abdominal pain (8% vs. 2%)
  - Diarrhea (7% vs. 2%)
  - Nausea (4% vs. 1%)
- Drug – drug interactions:
  - Avoid strong CYP3A inducers (rifampin, carbamazepine, St. John's wort, phenytoin) –decreased efficacy
  - Potentiated by moderate CYP3A inhibitors (diltiazem, fluconazole) and strong CYP3A inhibitors (clarithromycin, ketoconazole, ritonavir) – increased side effects

https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/208854s000lbl.pdf
Accessed 12-29-2017

Naldemedine

- Competition:
  - Methylnaltrexone (Relistor)
  - Naloxegol (Movantik)
- Advantages:
  - Another option to the market
  - Note: originally approved (3/2017) as Schedule II medication but descheduled by FDA in 9/2017
- Disadvantages:
  - Cost: $330.00 - $400.00 per month

https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/208854s000lbl.pdf
Accessed 12-29-2017

Plecanatide (Trulance)

- Class:
  - Guanylate cyclase-C agonist
- Indication:
  - Adults for treatment of chronic idiopathic constipation
- Dosage:
  - 3 mg taken orally once daily
  - With or without food; may be crushed and put in applesauce but not cut in 1/2

https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/208745lbl.pdf
Accessed 12-30-2017

Plecanatide

- Warnings and precautions:
  - The safety and effectiveness have not been established in patients less than 18 years of age (avoid use)
  - Diarrhea
  - Avoid in pregnancy and lactation
- Contraindications:
  - Contraindicated in patients less than 6 years of age; in young juvenile mice, plecanatide caused death due to dehydration

https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/208745lbl.pdf
Accessed 12-30-2017

Plecanatide

- Efficacy:
  - Approximately 1700 patients exposed to drug in clinical trials
  - Met Rome III criteria for chronic constipation
  - Responders (at least 3 or more CSBMs per week, an increase by at least 1 CSBM from baseline in 9 of 12 weeks, and at least 3 of last 4 weeks of study
    - 21% vs. 10%
    - 21% vs. 13%

https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/208745lbl.pdf
Accessed 12-30-2017

Plecanatide

- Side effects
  - Diarrhea (5% vs. 1%)
- Competition:
  - Linaclotide (Linzess)
  - Lubiprostone (Amitiza): different mechanism

https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/208745lbl.pdf
Accessed 12-30-2017

Plecanatide

- Drug – drug interactions:
  - No clinically significant drug-drug interactions
  - Is not metabolized through CYP or P-gp systems

https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/208745lbl.pdf Accessed 12-30-2017

Dermatology

Ozenoxacin (Xepi)

- New drug class: non-fluorinated quinolones
  - Inhibits bacterial DNA replication enzymes, DNA gyrase A, and topoisomerase IV
- 1% topical cream
- Approved for the treatment of impetigo
- 2 months of age and older
- Will be available first quarter of 2018

https://www.prnewswire.com/news-releases/medimetriks-pharmaceuticals-inc-receives-fda-approval-for-xepi-ozenoxacin-cream-1-a-novel-topical-antibiotic-for-impetigo-300571024.html accessed 12-30-2017

Ozenoxacin (Xepi)

- Apply two times daily x 5 days
- Trials:
  - 877 patients
  - Eradication: 90.8% versus 69.8% placebo
  - Excellent efficacy against: *MSSA, MRSA, and streptococcus pyogenes*
- No systemic absorption in 84/86 patients

https://www.prnewswire.com/news-releases/medimetriks-pharmaceuticals-inc-receives-fda-approval-for-xepi-ozenoxacin-cream-1-a-novel-topical-antibiotic-for-impetigo-300571024.html accessed 12-30-2017

New Fluoroquinolone

- Delafloxacin (Baxdela)
  - Indicated for adults with acute bacterial skin and skin structure infections (ABSSSI)
  - Activity against gram-positive and gram-negative pathogens, including MRSA.
  - Available in both intravenous and oral formulations as a monotherapy
  - 450 mg once daily – oral dosage

New

- Crisaborole ointment 2% (Eucrisa)
  - Nonsteroidal, topical PDE4 inhibitor
  - Mild – moderate atopic dermatitis
  - Apply two times daily to affected areas
  - 2 years of age and older
  - First PDE4 inhibitor (reduces cAMP)

Quick Updates

Updated Label

- Febuxostat (Uloric)
  - 40 mg daily is maximum dose for individuals with severe renal impairment (defined at CrCL < 30mL/min)
  - Mild to moderate renal impairment
    - No dosing adjustment

www.eMPR.com/news accessed 12-29-2017

ADHD Treatment

- Single entity amphetamine product (Mydayis)
  - Three different types of coated beads
  - Released at separate intervals
  - Duration of symptom control (16 hours)
  - 13 years of age and older
  - 12.5 or 25 mg once daily dosage
- Once daily extended release ODT formulation of methylphenidate (Contempla XR-ODT)
  - Ages 6 – 17 years
  - 12 hour of symptom control
  - 8.6 mg, 17.3 mg, and 25.9 mg strengths

New Formulation

- Valsartan (Prexxartan)
  - Liquid valsartan
  - Indication: Adults and children ages 6 years and older with hypertension, individuals with Class II – IV CHF) and to reduce the risk of cardiovascular death in individuals with left ventricular failure after MI
  - Unable to swallow pills
  - 4mg/mL strength solution

Additional New Approvals

- Cetirizine ophthalmic solution (Zerviate)
  - Allergic conjunctivitis
  - First cetirizine ophthalmic product
  - 0.24% once daily
  - 2 years of age and older

Triamcinolone acetonide: Extended-release injection

- Name: Zilretta
- Intra-articular injection
- Indication: OA knee pain
- Decreased pain x 12 weeks
- 32 mg injection
- First extended release injectable corticosteroid approved by FDA

Additional Approvals

- Tiotropium Bromide (Spiriva Respimat)
  - Indicated for asthma ages 6 – 11 years
- Ciprofloxacin and Gatifloxacin Ophthalmic
  - Bacterial conjunctivitis
  - Ages 1 month and older
  - Previously approved for 1 year of age and older

Pregabalin ER (Lyrica CR)

- Approved once daily for management of DPN and PHN
- Schedule V medication
- Dosages: 82.5 mg, 165 mg, 330 mg

New Labeling

- Budesonide/Formoterol (Symbicort)
  - Ages 6 – 12 years of age with asthma
- Fluticasone and salmeterol (AirDuo RespiClick)
  - Ages 12 years and older with asthma
- Lisdexamfetamine (Vyvanse)
  - Ages 6 years and older
  - Available in a chewable tablet
  - 10 mg, 20 mg, 30 mg, 40 mg, 50 mg, and 60 mg
- Lurasidone Hydrochloride (Latuda)
  - Adolescents ages 13 – 17 years
  - Indication: schizophrenia or irritability associated with autistic disorder

Triple Drug Inhaler

- Fluticasone furoate, umeclidinium, and vilanterol (ICS, LAMA, LABA)
  - Trelegy Ellipta
  - COPD indication only
  - 1 puff daily
  - Boxed warning: LABA use may be associated with increased risk of asthma related death

New Approvals

- Zolmitriptan (Zomig Nasal Spray)
  - Acute treatment of migraine in children 12 – 17 years of age
  - 1 spray into one nostril x 1
  - 2.5 mg per spray
  - Maximum: 10 mg in 24 hours

What's coming?

- CM4620 (acute pancreatitis)
- Metoclopramide nasal spray (diabetic gastroparesis in women)
- Galcanezumab (CGRP inhibitor) once monthly sc injection for prevention of chronic migraines (three products currently pending approval or in phase 3 trials)

Immunizations

HPV 9

- NEW APPROVAL
  - Ages 9 – 14 years: 2 dose series
    - Day 0 and day 6 months
  - Ages 15 – 26 years: 3 dose series

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Additional Recommendations

- Hepatitis B series
  - All individuals with liver disease
  - Including fatty liver, cirrhosis, alcoholic liver disease
  - All individuals with ALT or AST > 2 x upper limits of normal

Hepatitis B Vaccine Approved

- Hepatitis B vaccine (Heplisav-B)
  - 18 years of age and older
  - Label will show seroprotection superiority to current Hepatitis B vaccine (Engerix-B)
    - Ages 18 – 55 years (95% vs. 81.3%)
    - Ages 40 – 70 years (90.1% vs. 70.5%)
  - 2 dose series
  - Day 0 and Day 1 month
  - Launch: First quarter 2018

Approved October 2017

- Vaccine
  - Herpes zoster vaccine (Shingrix)
  - Ages 50 years and older
  - Non-live vaccination
  - 90% efficacy (independent of age 50 - > 80 years)
  - Sustained efficacy over 4 years
  - Two dose vaccine
  - Day zero and day 2 months – 6 months

October 2017

- Herpes zoster
  - Will be available first quarter of 2018
  - Now preferred over previous herpes zoster vaccine (Zostavax)
  - All individuals who have received previous vaccine should receive this vaccine
  - Age dropped to 50 years of age to align with the FDA approval for vaccination

Thank you!
I would be happy to entertain any questions or comments

Wendy L. Wright,
MS, ANP-BC, FNP-BC, FAANP, FAAN, FNAP
WendyARNP@aol.com