A Year in Review: Novel Drug Approvals

Robin Parker, PharmD
Assistant Professor of Pharmacy Practice
Lipscomb University College of Pharmacy
robin.parker@lipscomb.edu

Objectives

1. Identify the clinical indications for new FDA approved drugs for the past year.
2. Describe the mechanism of action (MOA) and potential contraindications for each new medication
3. Identify common adverse reactions (ADE) associated with the discussed medications
4. Describe significant drug interactions for the reviewed medications

Drug approvals in 2017

- The FDA has approved 29 novel new drugs and biologics through the end of August of 2017

- Areas of approval include dermatology, hematology, oncology, infectious diseases, and more

generic (BRAND)

- Indication:
- Mechanism of action:
- Clinical trial information:
- Scheduling information:
- Dosing:
- Adverse drug reactions:
- Contraindications:
- Counseling points:

Name of Medicine [package insert]. Place of publication : Publisher; Year of publication.

RED BOOK:
WAC $

Dermatology

brodalumab (SILIQ)

- Moderate-to-severe plaque psoriasis
- MOA: IL-17 receptor A blocker
- Three placebo-controlled trials in over 4,000 patients established efficacy
- Rx: 210mg subQ every 2 weeks in a prefilled syringe
- ADR: joint pain, headache, fatigue, diarrhea, throat pain
- BBW: suicidal ideation and behavior
  - REMS program/specialty pharmacies
- CI: Crohn's disease
- Counseling: watch for mood changes (wallet card), infection risk, allow injection to come to room temperature before injection; 16 week response window

Siliq [package insert]. Bridgewater, NJ: Valeant; 2017.

RED BOOK:
WAC $3,500.00 per month

dupilumab (DUPIXENT)

- Moderate-to-severe atopic dermatitis
- MOA: IL-4 and IL-13 blocking monoclonal antibody
- Approval comes after three placebo-controlled efficacy trials
  - Participants had wide-spread rashes (~1/2 body surface)
  - Clear or almost clear skin with decreased itching after 16 weeks of therapy
- Rx: 300mg/2mL subQ injection every other week
  - Prefilled syringe; refrigeration required
- ADR: injection site reactions, cold sores, conjunctivitis
- Counseling: Allow the injection to come to room temperature prior to administration; notify provider of eye issues

Dupixent [package insert]. Tarrytown, NY: Regeneron; 2017.

RED BOOK:
WAC $2,846.16 for 2 doses

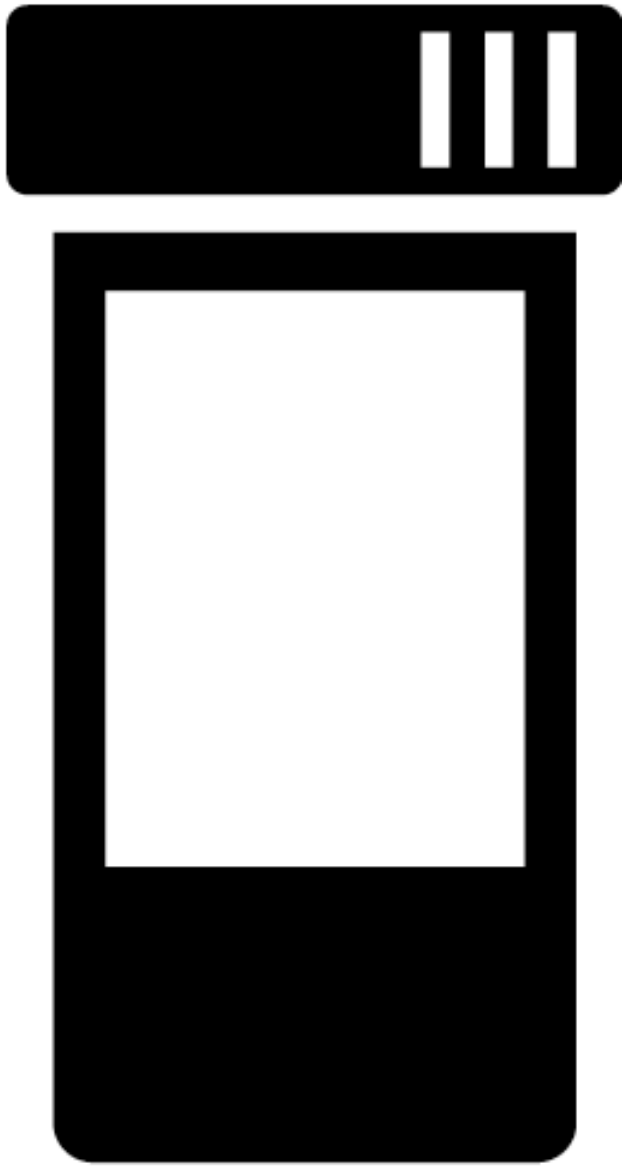
guselkumab (TREMFYA)

- Moderate-to-severe plaque psoriasis
- MOA: selective IL-23 blocker
- Approval based on three phase 3 trials in more than 2,000 patients
  - Psoriasis Area and Severity Index score improvements along with symptom improvement with results maintained at week 48
- Rx: 100mg subQ every 8 weeks in a prefilled syringe
- ADR: infections, headache, injection site reactions, joint pain, diarrhea
- Counseling: infection risk, allow injection to come to room temperature before injection

Tremfya [package insert]. Horsham, PA: Janssen; 2017.

RED BOOK:
WAC $9,684.00 per injection

Endocrinology



abaloparatide (TYMLOS)

- Postmenopausal women with osteoporosis at high risk for fracture
- MOA: parathyroid hormone receptor-1 agonist
- Approval comes after the ACTIVE and ACTIVExtend trials
  - Significant reductions in RR for new vertebral and nonvertebral fractures
- Rx: 80mcg subQ once daily into periumbilical region
  - Supplemental calcium and vitamin D if dietary intake is inadequate
- ADR: injection site reactions, hypercalciuria, dizziness, orthostatic hypotension, hypercalcemia
- BBW: risk of osteosarcoma
- Counseling: Refrigerate pen, cumulative use for more than 2 years is not recommended

Tymlos [package insert]. Waltham, MA: Radius; 2017.

RED BOOK:
WAC $1,625.00 per month

etelcalcetide (PARSABIV)

- Secondary hyperparathyroidism in CKD patients on dialysis
- MOA: calcimimetic
- Approval based on two trials where the majority of patients achieved 30% PTH reduction from baseline during weeks 20-27
- Rx: 5mg IV bolus 3x weekly at end of dialysis
  - Adjustments based on PTH and serum calcium response
- ADR: hypocalcemia, muscle spasms, GI issues, worsened HF
- Counseling: stop cinacalcet at least 7 days prior to first dose; monitor for symptoms of hypocalcemia or worsening HF

Parsabiv [package insert]. Thousand Oaks, CA: Amgen; 2017.

RED BOOK:
Pricing info not available

Gastroenterology

naldemedine (SYMPROIC)

- Opioid-induced constipation in chronic, non-cancer pain
- MOA: peripherally-acting mu opioid receptor antagonist
- Approval obtained through the COMPOSE I-III trials
- Schedule II controlled substance
- Rx: 0.2mg oral tablet once daily
- ADR: abdominal pain, diarrhea, nausea
- Avoid in those with GI obstruction
- Counseling: discontinue use if opioids are stopped

Symproic [package insert]. Florham Park, NJ: Shionogi; 2017.

RED BOOK:
Pricing info not available

plecanatide (TRULANCE)

- Chronic idiopathic constipation
- MOA: Guanyl cyclase C agonist, which increases cGMP to increase intestinal fluid and motility
- Two placebo-controlled trials demonstrated increased complete spontaneous bowel movements as compared to placebo
  - Participants also noted improved stool frequency, consistency, and straining
- Rx: 3mg oral tablet daily
- ADR: diarrhea
- Avoid in those under 6 years of age and those with GI obstruction
- BBW: dehydration risk in pediatric patients
- Counseling: keep tablets dry and do not remove desiccant from bottle

Trulance [package insert]. New York, NY: Synergy; 2017.

RED BOOK:
WAC $353.48 per month

Neurology

cerliponase alfa (BRINEURA)

- To slow loss of ambulation in late infantile neuronal ceroid lipofuscinosis type 2 (CLN2) in those ages 3 and older
- MOA: recombinant TPP1 enzyme
- Efficacy demonstrated in an open-label study involving 22 children
  - Treated patients had fewer declines in walking ability compared to a natural history cohort
- Rx: 300mg infused into CSF every other week
- ADR: fever, ECG abnormalities, hypersensitivity, vomiting, seizures
- CI: access complications, ventriculoperitoneal shunts
- Counseling: hypotension or bradycardia may occur after infusion, watch for signs of infection

Brineura [package insert]. Novato, CA: BioMarin; 2017.

RED BOOK:
WAC $54,000.00 per infusion

deflazacort (EMFLAZA)

- Duchenne muscular dystrophy in patients 5 years and older
- MOA: corticosteroid
- Effectiveness seen in trial of 196 boys with DMD ages 5-15 years
  - Improvements in muscle strength noted compared to placebo
- Rx: 0.9 mg/kg/day by mouth once daily
  - Available in tablet and liquid forms
- ADR: Cushingoid appearance, weight gain, increased appetite, URTI, cough, pollakiuria, hirsutism, central obesity, nasopharyngitis
- Counseling: do not give with grapefruit juice, if stopping deflazacort, taper appropriately

Emflaza [package insert]. Northbrook, IL: Marathon; 2017.

RED BOOK:
WAC $3,925.00 per month

deutetrabenazine (AUSTEDO)

- Treatment of chorea associated with Huntington's disease
- MOA: vesicular monoamine transporter 2 (VMAT2) inhibitor
- Efficacy demonstrated in multiple scaled-score improvements
- Rx: 12mg BID with food
  - Requires individualization to each patient
- ADR: drowsiness, diarrhea, dry mouth, fatigue
- Contraindicated in those with uncontrolled/untreated depression, liver impairment, or concurrent MAOI, reserpine, or tetrabenzine use
- BBW: risk for depression and suicidal thoughts and behaviors
- Counseling: report arrhythmias; see medication impact before activities requiring mental alertness

Austedo [package insert]. North Wales, PA: Teva; 2017.

RED BOOK:
WAC $4,932.00 per month

edaravone (RADICAVA)

- To slow functional decline in amyotrophic lateral sclerosis (ALS)
- MOA: unknown; pyrazolone free-radical scavenger
- Effectiveness based on 6-month trial in Japan in 137 patients
  - Week 24 revealed less decline in those who received edaravone versus placebo
- Rx: 60mg IV infusion daily for 14 days, followed by 14 days with no treatment; cycles repeat
- ADR: bruising, gait disturbances
- Counseling: potential sulfite sensitivity

Radicava [package insert]. Jersey City, NJ: Mitsubishi; 2017.

RED BOOK:
WAC $1,086.00 per infusion

ocrelizumab (OCREVUS)

- Relapsing or primary progressive forms of MS
- MOA: monoclonal antibody targeting CD20 antigens on B cells
- Trials revealed reduced rates of disease progression compared to placebo and interferon b-1a
  - 25-foot walk test, brain lesion volume, percentage brain-volume loss
- Rx: 600mg IV infusion every 6 months
  - Premedicate with a corticosteroid and antihistamine prior to infusion
- ADR: infusion site reactions (up to 24-hours post-infusion), infections
- Contraindicated in those with active HepB infection
- Counseling: watch for signs of infusion reaction

Ocrevus [package insert]. San Francisco, CA: Genentech; 2017.

RED BOOK:
WAC $16,250.00 per 300mg

safinamide (XADAGO)

- Adjunctive treatment to levodopa/carbidopa in patients with Parkinson's disease
- MOA: selective MAO-B inhibitor
- Clinical trials in patients experiencing "off-time" showed increases in "on time" when safinamide was added compared to placebo
  - Also saw better scores on a measure of motor function
- Rx: 50mg once daily by mouth
  - May increase to 100mg QD if needed/tolerable
- ADR: dyskinesia, falls, nausea, insomnia
- CI: risk of serotonin syndrome with use of MAOIs, opioids, SNRIs, amphetamines, cyclobenzaprine; severe hepatic impairment
- Counseling: report excessive drowsiness or impulse control; avoid tyramine-containing foods

Xadago [package insert]. Louisville, KY: US WorldMeds; 2017.

RED BOOK:
WAC $669.90 per month

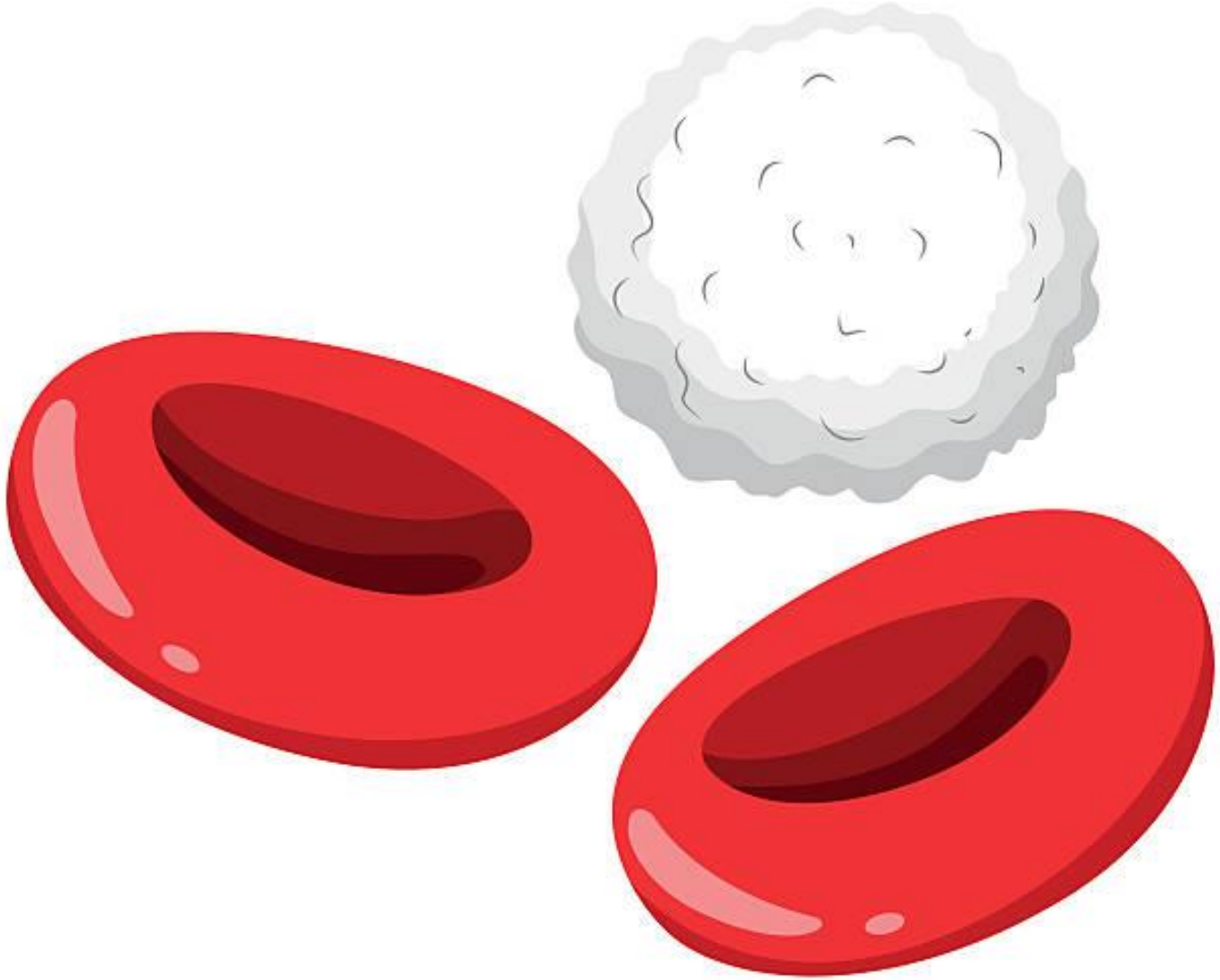
valbenazine (INGREZZA)

- Tardive dyskinesia
- MOA: vesicular monoamine transporter 2 (VMAT2) inhibitor
- Approval based on results from multiple studies noting significant improvements in TD symptoms at 6 weeks
- Rx: 40mg by mouth once daily
  - Can increase to 80mg once daily
- ADR: somnolence, dry mouth, constipation, vomiting, nausea
- Counseling: avoid activities requiring mental alertness until effects are known, watch for arrhythmias

Ingrezza [package insert]. San Diego, CA: Neurocrine; 2017.

RED BOOK:
WAC $5,275.00 per month

Hematology



betrixaban (BEVYXXA)

- Venous thromboembolism prophylaxis in hospitalized, acutely-ill, mobility-restricted patients
- MOA: factor Xa inhibitor
- APEX trial compared betrixaban versus enoxaparin in 7,513 patients
  - Fewer events seen with betrixaban (4.4%) compared to enoxaparin (6%); RR 0.75 (95% CI, 0.61-0.91) with similar bleeding rates
- Rx: 80mg once daily with food for 35-42 days
- ADR: bleeding (epistaxis, hematuria), UTI, constipation, HTN, headache
- CI: active bleeding
- Counseling: take with food at the same time daily; do not double doses if it is close to next dose

Bevyxxa [package insert]. San Francisco, CA: Portola; 2017.

RED BOOK:
Pricing info not available

L-glutamine (ENDARI)

- To reduce complications in sickle cell disease in those 5 years and older
- MOA: not fully understood; antioxidant activity
- Data from a randomized trial with patients aged 5 to 58 years with 2+ pain crises within the past year revealed efficacy
  - Those who received L-glutamine experienced fewer pain-related hospital visits, fewer pain hospitalizations, and fewer hospitalized days
- Rx: 5-15g oral power mixed with beverage or food twice daily
  - Weight-based dosing
- ADR: constipation, nausea, headache, abdominal pain, cough, back pain
- Counseling: do not double doses, take missed doses as soon as possible; mix in cool or room temperature substance

Endari [package insert]. Torrance, CA: Emmaus; 2017.

RED BOOK:
WAC $497.00 per month

Oncology

avelumab (BAVENCIO)

- Metastatic Merkel cell carcinoma in those 12 and older; now approved for patients with advanced or metastatic urothelial carcinoma
- MOA: Anti-PD-L1 IgG1 monoclonal antibody
- Received accelerated approval on the basis of response rates from a single-arm clinical trial conducted in 88 patients with chemotherapy-refractory MCC
- Rx: 10mg/kg IV infusion every 2 weeks
  - Premedicate with acetaminophen and antihistamines prior to infusion
- ADR: fatigue, infusion-related reactions, muscle pain, diarrhea, nausea, decreased appetite
- Counseling: females should avoid pregnancy; report any immune-mediated adverse reactions

Bavencio [package insert]. Rockland, MA: EMD Serono; 2017.

RED BOOK:
WAC $1504.00 per 200mg

brigatinib (ALUNBRIG)

- ALK-positive metastatic non-small cell lung cancer
- MOA: tyrosine-kinase inhibitor
- Approval based on overall response rates
  - Median duration of response was 13.8 months
- Rx: 180mg by mouth once daily
- ADR: nausea, diarrhea, fatigue, cough, headache
- Counseling: if a dose is missed or vomited, do not take an extra dose, but to take the next dose at the regular time; report any worsening respiratory symptoms or visual disturbances

Alunbrig [package insert]. Cambridge, MA: Ariad; 2017.

RED BOOK:
WAC $14,250.00 per month

durvalumab (IMFINZI)

- Advanced or metastatic urothelial carcinoma
- MOA: monoclonal antibody that blocks PD-L1 binding with PD-1 and CD80
- Approval based on a single-arm trial in 182 patients
  - Target lesion diameter objective response rate was 17%
- Rx: 10mg/kg IV infusion every 2 weeks
- ADR: fatigue, infection, musculoskeletal pain, constipation, rash
- Counseling: infusion-related reactions/infections, watch for symptoms of hepatitis, colitis, pneumonitis

Imfinzi [package insert]. Wilmington, DE: AstraZeneca; 2017..

RED BOOK:
WAC $834.92 per 50mg/mL

enasidenib (IDHIFA)

- Relapsed or refractory AML with an IDH2 mutation
- MOA: targeted inhibitor of the IDH2 enzyme
- Approval based on a single-group trial of 199 patients
  - 19% of patients experienced full recovery of blood counts; 4% partial recovery
- Rx: 100mg by mouth once daily
- ADR: nausea, vomiting, diarrhea, elevated bilirubin, decreased appetite
- BBW: differentiation syndrome
- CI: pregnant/breast feeding women
- Counseling: avoid pregnancy; watch for symptoms of differentiation syndrome; if dose is missed/vomiting, take as soon as possible on same day, skip missed dose if an entire day has passed

Idhifa [package insert]. Summit, NJ: Celgene; 2017.

RED BOOK:
WAC $24,872.00 per month

inotuzumab ozogamicin (BESPONSA)

- Relapsed or refractory acute lymphoblastic leukemia
- MOA: CD22-directed antibody-drug conjugate
- INO-VATE ALL open-label trial randomized 326 patients had more in the inotuzumab ozogamicin arm achieve complete remission compared to the alternative chemotherapy arm
  - 35.8% versus 17.4%, respectively
- Rx: weight-based dosing dependent on cycle
- ADR: thrombocytopenia, neutropenia, infection, anemia, leukopenia, fatigue, hemorrhage, pyrexia, nausea, headache, febrile neutropenia, increases in transaminase level, abdominal pain, increases in gamma-glutamyltransferase level, and hyperbilirubinemia
- Counseling: report symptoms of infection, arrhythmia, infusion-related reactions, and hepatotoxicity; avoid pregnancy

Besponsa [package insert]. Philadelphia, PA: Wyeth; 2017.

RED BOOK:
WAC $18,700.00 per 0.9mg

midostaurin (RYDAPT)

- Acute myeloid leukemia with the FLT3 genetic mutation
- MOA: kinase inhibitor
- Clinical studies in 717 patients with AML led to approval
  - Patients treated with midostaurin lived longer
- Rx: 50mg by mouth twice daily with food on days 8-21
- ADR: febrile neutropenia, nausea, mucositis, vomiting, headache, pain, petechiae, epistaxis
- Counseling: avoid pregnancy during therapy and for at least 4 months after; report any respiratory changes; if a dose is missed or vomited, do not take an extra dose, but take the next dose at the regular time

Rydapt [package insert]. East Hanover, NJ: Novartis; 2017.

RED BOOK:
WAC $3,747.50 per cycle

neratinib (NERLYNX)

- Extended adjuvant treatment of adult patients with early stage HER2-overexpressed/amplified breast cancer
- MOA: kinase inhibitor
- Approval based on phase 3 trial data in over 2800 patients
  - After 2 years, patients treated with 1 year of neratinib had a disease-free survival compared to placebo (94.2% versus 91.9%, respectively)
- Rx: 240mg by mouth once daily with food
- ADR: diarrhea, nausea, abdominal pain, fatigue, vomiting, rash, stomatitis, decreased appetite, muscle spasms, dyspepsia, liver damage
- Counseling: report severe diarrhea; avoid pregnancy during and after treatment; skip missed doses; avoid with grapefruit products

Nerlynx [package insert]. Los Angeles, CA: Puma; 2017.

RED BOOK:
WAC $10,500.00 per month

niraparib (ZEJULA)

- Maintenance treatment of recurrent ovarian, fallopian tube, or primary peritoneal cancers
- MOA: poly ADP-ribose polymerase (PARP) inhibitor
- Approval based on results from the NOVA trial
  - Significant improvement in progression-free survival with niraparib versus placebo
- Rx: 300mg by mouth once daily
- ADR: thrombocytopenia, anemia, neutropenia, leukopenia, palpitations, nausea, constipation, vomiting, abdominal pain/distention, mucositis/stomatitis, diarrhea, dyspepsia, dry mouth, fatigue, decreased appetite, urinary tract infection, AST/ALT elevation, myalgia, back pain, arthralgia, headache, dizziness, dysgeusia, insomnia, anxiety, nasopharyngitis, dyspnea, cough, rash, and hypertension
- Counseling: if patient misses/vomits a dose to skip the missed dose and resume a normal schedule

Zejula [package insert]. Waltham, MA: Tesaro; 2017.

RED BOOK:
WAC $14,750.00 per month

ribociclib (KISQALI)

- HR-positive, HER-2 negative advanced or metastatic breast cancer in combination with an aromatase inhibitor
- MOA: cyclin-dependent kinase-4 and -6 inhibitor
- Approval based on MONALEESA-2 study results in 668 women
  - ribociclib plus letrozole reduced the risk for progression or death by 44% over letrozole alone (HR 0.556, 95% CI 0.429-0.720]; p<0.0001)
- Rx: 600mg orally once daily for 21 days
- ADR: neutropenia, nausea, fatigue, diarrhea, leukopenia, alopecia
- Counseling: QT interval prolongation, hepatobiliary toxicity, monitoring requirements

Kisqali [package insert]. New Hanover, NJ: Novartis; 2017.

RED BOOK:
WAC $10,950.00 per cycle

telotristat ethyl (XERMELO)

- Indicated for carcinoid syndrome diarrhea in combination with somatostatin analog therapy
- MOA: tryptophan hydroxylase inhibitor
- Efficacy established in a double-blind, placebo-controlled randomized trial in 90 patients having between 4-12 bowel movements daily
  - 33% in the telotristat-plus-SSA group had an average reduction of two BM per day compared with just 4% of the placebo-plus-SSA group
- Rx: 250mg orally three times daily with food
- ADR: nausea, headache, increased levels of the liver enzyme gamma-glutamyl transferase, depression, peripheral edema, flatulence, decreased appetite, fever
- Counseling: may cause constipation; do not double doses

Xermelo [package insert]. Woodlands, TX: Lexicon; 2017.

RED BOOK:
WAC $5,164.00 per month

Rheumatology

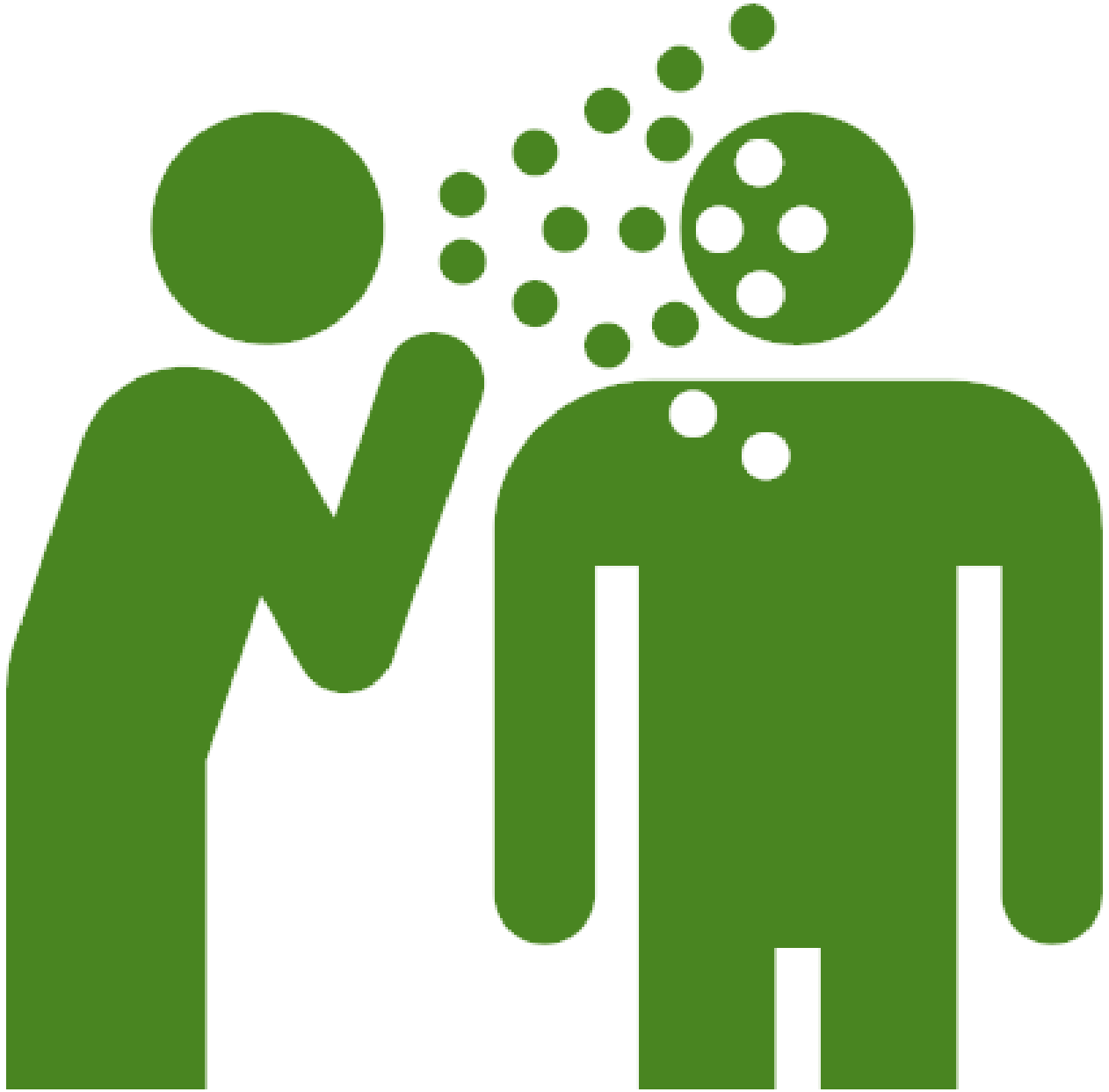
sarilumab (KEVZARA)

- Moderately to severely active rheumatoid arthritis
- MOA: interleukin-6 blocker
- Approval comes after improvements noted in 2,900 patients
  - reduced s/s, improved physical function, less structural damage
- Rx: 200mg subQ every two weeks in a prefilled syringe
- ADR: neutropenia, elevated liver enzymes, injection site reaction, infections
- BBW: infections
- Counseling: refrigerate syringe; allow to come to room temp prior to injection

Kevzara [package insert]. Bridgewater, NJ: Sanofi-Aventis; 2017.

RED BOOK:
WAC $3,000.00 per month

Infectious Disease



delafloxacin (BAXDELA)

- Acute bacterial skin and skin structure infections
- MOA: Fluoroquinolone that inhibits bacterial topoisomerase IV and DNA gyrase (topoisomerase II) enzymes
- Determined to be safe and effective based on two randomized trials in 1,500 adults with ABSSSIs that compared with an IV combination of vancomycin plus aztreonam
  - Similar efficacy noted between the two treatments
- Rx: 300mg IV or 450mg orally every 12 hours for 5-14 days
- ADR: nausea, diarrhea, headache, increased transaminases, vomiting
- BBW: adverse reactions
- Counseling: take missed dose within 8 hours, skip if longer than 8 hours

Baxdela [package insert]. Lincolnshire, IL: Milenta; 2017.

RED BOOK:
Pricing info not available

glecaprevir/pibrentasvir (MAVYRET)

- Chronic HCV genotypes 1 through 6 without cirrhosis or with mild cirrhosis
- MOA: NS3/4A protease inhibitor and NS5A replication complex inhibitor
- Deemed safe and effective based on clinical trials involving 2300 adults
  - Between 92-100% of patients had no detectable virus after 12 weeks
- Rx: 3 tablets by mouth once daily with food for 8-16 weeks
- ADR: headache, fatigue, nausea
- BBW: hepatitis B virus reactivation
- CI: severe hepatic impairment; concomitant use with rifampin or atazanavir
- Counseling: take a missed dose as soon as possible if the delay is less than 18 hours after the scheduled dose; if the delay is longer than 18 hours, skip the missed dose and resume normal schedule

Mavyret [package insert]. Chicago, IL: Abbvie; 2017.

RED BOOK:
WAC $13,200.00 per month

sofosbuvir/velpatasvir/voxilaprevir (VOSEVI)

- Chronic hepatitis C infection types 1-6 without cirrhosis or with mild cirrhosis
- MOA: NS5B polymerase inhibitor, NS5A inhibitor, and NS3/4A protease inhibitor
- Safety and efficacy proven in two phase 3 trials in 750 adults
  - Results demonstrated 96-97% of patients who received Vosevi sustained viral response at 12 weeks
- Rx: 1 tablet by mouth once daily for 12 weeks
- ADR: headache, fatigue, diarrhea, nausea
- BBW: hepatitis B virus reactivation
- CI: concomitant rifampin use
- Counseling: take 4 hours apart from antacids; report symptoms of bradycardia

Vosevi [package insert]. Foster City, CA: Gilead; 2017.

RED BOOK:
WAC $24,920.00 per month

Questions?

Robin Parker, PharmD
Assistant Professor of Pharmacy Practice
Lipscomb University College of Pharmacy
robin.parker@lipscomb.edu