

New and Notable Medications Approved in 2010 and 2011

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Learning Objectives

At the conclusion of this lesson, successful participants should be able to:

1. recall recent novel drug therapies that are expected to significantly impact future practice.
2. review the pharmacology of newly approved drug therapies.
3. become familiar with Food and Drug Administration-approved indications, contraindications, warnings/precautions and pertinent counseling points.
4. identify the role of these medications in disease management and indicated disease states.

Introduction

The number of new molecular entities (defined as chemical substances unique from currently marketed and regulated drugs) in development for commercial use has been steadily decreasing over the past 15 years. Yet, several new medications recently approved will noticeably change practice.¹ This article highlights the most interesting and influential agents recently approved, providing a brief overview of the agent and relevant information based on the practice setting in which it is most likely to be used (e.g., a health-system versus a community pharmacy). A list of medications approved in 2010 through September 2011 is provided (Appendices A and B). The intent of this review is to provide a brief introduction to these agents rather than a comprehensive, detailed description of each.

Agents Approved in 2010					
Generic Name*	Brand Name*	Manufacturer†	Use*	New/Notable	Cost (AWP)‡
Fingolimod	Gilenya™	Novartis Pharmaceuticals Corporation	Indicated for the treatment of patients with relapsing forms of multiple sclerosis to reduce the frequency of relapses and to delay the accumulation of physical disability	First oral medication for relapsing multiple sclerosis	\$4,426.24 0.5 mg #28
Dabigatran Etexilate	Pradaxa™	BoehringerIngelheim Pharmaceuticals, Inc.	Indicated to reduce the risk of stroke and systemic embolism in patients with non-valvular atrial fibrillation	First oral anticoagulant since the discovery of warfarin more than 50 years ago	\$262.44 75 mg or 150 mg #60
Ceftaroline Fosamil	Teflaro™	Forest Pharmaceuticals, Inc.	IV cephalosporin for skin and skin structure infections and community-acquired pneumonia	First beta-lactam to cover Methicillin-resistant staphylococcus aureus (MRSA)	\$492 400 mg or 600 mg #10 (vials)

Agents Approved in 2011					
Generic Name*	Brand Name*	Manufacturer†	Use*	New/Notable	Cost (AWP)‡
Rivaroxaban	Xarelto™	Janssen Pharmaceuticals	To reduce the risk of blood clots following knee or hip replacement surgery	Oral Factor Xa inhibitor; first approved in the United States	\$243 10 mg #30
Fidaxomicin	Dificid™	Optimer Pharmaceuticals, Inc.	For the treatment of <i>Clostridium difficile</i> -associated diarrhea (CDAD)	First antibiotic in its class; activity against hypervirulent strains of <i>C. difficile</i>	\$3,360 200 mg #20
Belimumab	Benlysta™	Human Genome	To treat patients with	First approved	\$531.82

		Sciences, Inc. (GlaxoSmithKline Group of Companies)	active, autoantibody- positive lupus who are receiving standard therapy, including corticosteroids, antimalarial agents, immunosuppressive agents and nonsteroidal anti- inflammatory drugs	medication for systemic lupus erythematosus(SLE) in approximately 50 years	120 mg (vial) \$1,772.71 400 mg (vial)
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* obtained from United States Food and Drug Administration

† obtained from respective product package inserts

Agents Approved by the Food and Drug Administration (FDA) in 2010

Fingolimod (Gilenya™)

Fingolimod is an oral therapy for relapsing-remitting multiple sclerosis with a novel mechanism of action. It is the first sphingosine-1 receptor antagonist and it is also the first oral medication approved to manage multiple sclerosis (MS). Sphingosine-1 receptors are found on lymphocytes. Fingolimod is thought to inhibit these receptors, which leads to sequestration in lymph nodes, thus reducing lymphocyte-mediated auto-immune destruction of myelin in multiple sclerosis flares.

Fingolimod was first described in 1995 when it was derived from fungal myriocin metabolites. It preferentially interacts with the sphingosine 1-phosphate (S1P) receptors on lymphocytes in the periphery. This receptor appears to play key roles in immune cell trafficking, angiogenesis and endothelial function.² T cells are initially mobilized upon introduction of fingolimod. Through an additional mechanism that is not yet described, it is thought that fingolimod causes these cells to internalize the S1P receptors, thus acting as a functional antagonist. With fingolimod-mediated receptor down regulation, the ability of endogenous sphingosine to activate these cells is reduced. Once steady state concentrations of fingolimod are reached, lymphocyte count stabilizes at approximately 60 percent of baseline. Lymphocyte activity is restored upon cessation of therapy.³

Fingolimod may provide a direct benefit on oligodendrocytes in the central nervous system. *In vitro* exposure to fingolimod has been reported to increase both the concentrations of progenitor and mature oligodendrocytes. It is also believed that fingolimod protects these cells from cytokine-induced cell death.⁴ Fingolimod may offer further benefits by activating astrocytes, which play a role in neuronal repair. In the acute phase of neuronal injury, astrocytes limit inflammatory response while protecting oligodendrocytes and axonal regeneration.⁵

The safety and efficacy of fingolimod were demonstrated in two large phase III trials: TRANSFORMS and FREEDOMS. TRANSFORMS was a 12-month study evaluating daily oral fingolimod against weekly interferon beta-1a injections in relapsing-remitting multiple sclerosis patients. Fingolimod achieved a 52 percent reduction in annualized relapse rate with 83 percent remaining relapse-free after one year. FREEDOMS was a 24-month trial of relapsing-remitting MS

Fingolimod Patient Counseling Points

Common side effects include:

- Headache, cough, diarrhea, back pain and increase in transaminase

Serious side effects may include:

- **Slow heart rate (brady arrhythmia):** tell your doctor immediately if you experience fainting, dizziness, unusual tiredness or a noticeably slow heartbeat.
- **Infections:** signs of infection usually include more than one of the following symptoms - tiredness, nausea, fever, body aches, chills or vomiting. Inform your doctor if you experience these symptoms.
- **Macular edema:** macular edema is a rare but serious condition caused by fluid accumulation within the eye. Symptoms include blurry vision, light sensitivity or blind spots. Inform your doctor if you experience these symptoms.

patients that compared fingolimod to placebo. Fingolimod achieved a 55 percent reduction in relapse at 24 months with 70 percent of patients remaining relapse-free.^{6,7}

Patients starting on fingolimod should be observed for six hours after the first dose. Fingolimod can cause transient brady-arrhythmia and potential atrial-ventricular blocks during its induction phase. There may also be an additive effect with beta blockers or antiarrhythmic medications. Once steady state concentrations are reached at 1-2 months, some patients may experience a small increase in systolic blood pressure, usually less than 5mm Hg. As with any immunomodulator, patients receiving fingolimod may be at an increased risk of infection, although this was not observed in clinical trials.

Avoid use of fingolimod for two months prior to administering live vaccines. Concomitant administration with ketoconazole, an inhibitor of CYP4F and 3A4, increases fingolimod concentrations by 70 percent which can increase the likelihood for adverse effects.⁸ Fingolimod has not been studied in pregnant or nursing mothers and considerable caution should be employed by providers or patients considering use in this population.⁹

Dabigatran Etexilate (Pradaxa™)

Dabigatran etexilate is probably the most well-known new molecular entity approved by the FDA within the last two years. Its approval in October 2010 marked the first time in decades that a new oral anticoagulant was approved to reduce the risk of stroke and systemic embolism in patients with nonvalvular atrial fibrillation. Warfarin, the other oral anticoagulant, was approved by the FDA in 1954.¹⁰

Dabigatran is a direct thrombin inhibitor. Thrombin, factor II in the coagulation cascade, plays an integral and multi-functional role in hemostasis. Its main role is to convert fibrinogen to fibrin; but it also provides feedback on the clotting cascade to activate factors V and VIII that allow for subsequent thrombin generation. Together, these actions result in clot formation and the promotion of platelet adhesion.¹¹ Unlike warfarin, dabigatran does not require international normalized ratio (INR) monitoring because of its consistent dose-response effects, which makes this an attractive alternative.

While advantageous from a therapeutic monitoring perspective, there is no sufficiently sensitive method to monitor levels and no specific antidote in the event of an overdose. The most sensitive method of monitoring anticoagulant activity is ecarin clotting time. The most accessible method is activated partial thromboplastin time, but it is not precise.¹²

In the pivotal trial that led to its FDA approval [Dabigatran versus Warfarin in Patients with Atrial Fibrillation, from the members of the Randomized Evaluation of Long-Term Anticoagulation Therapy (RE-LY) Study Group], dabigatran proved favorable. The study evaluated close to 20,000 patients with atrial fibrillation and risk of stroke and compared adjusted-dose warfarin to either 110 mg or 150 mg twice daily dabigatran. Each dose of dabigatran was noninferior to warfarin with respect to the primary outcome of stroke and systemic embolism, and the 150 mg dose was actually found to be superior. Rates of hemorrhagic complications were significantly lower for each dabigatran dose; however, the rate of gastrointestinal bleeding was higher in the 150 mg dabigatran group. Dyspepsia was the only adverse event reported more commonly in the dabigatran group when compared to the warfarin group.^{13,14}

Dosing of dabigatran is based on renal function. In patients with creatinine clearance (CrCl) > 30 mL/min, the dose is 150 mg orally twice daily. In patients with CrCl between 15-30 mL/min, the dose is 75 mg orally twice daily. Dabigatran is not recommended in patients with CrCl less than 15 mL/min or on dialysis. Since most patients eligible for dabigatran are also candidates for warfarin therapy, and are likely to be bridged from parenteral anticoagulants, the manufacturer provides instruction for converting between agents (see Table 1).¹⁵ Dabigatran must be dispensed in either the



original packaging or in blister packs. The medication is sensitive to moisture and once the bottle is opened, it must be used within 30 days.^{16,17}

Table 1. Directions for Converting Between Dabigatran and Similar Agents

Converting patients from warfarin to dabigatran	Discontinue warfarin and start dabigatran when the international normalized ratio (INR) is below 2.0
Converting from dabigatran to warfarin	Adjust the starting time of warfarin based on creatinine clearance (CrCl): <ul style="list-style-type: none"> • CrCl > 50 mL/min, start warfarin three days before discontinuing dabigatran • CrCl 31-50 mL/min, start warfarin two days before discontinuing dabigatran • CrCl 15-30 mL/min, start warfarin one day before discontinuing dabigatran • CrCl < 15 mL/min, no recommendations can be made
Converting from parenteral anticoagulants to dabigatran	Start dabigatran 0-2 hours before the time that the next dose of the parenteral drug was to have been administered, or at the time of discontinuation of a continuously administered parenteral drug
Converting from dabigatran to parenteral anticoagulants	Wait 12 hours (CrCl ≥ 30 mL/min) or 24 hours (CrCl < 30 mL/min) after the last dose of dabigatran before initiating treatment with a parenteral anticoagulant

Ceftaroline Fosamil (Teflaro™)

Ceftaroline fosamil is a broad-spectrum cephalosporin that represents a paradigm shift because it is the first beta-lactam that is able to provide coverage against *Methicillin-resistant staphylococcus aureus* (MRSA). Its current FDA indications include the treatment of acute bacterial skin and skin structure infections (ABSSSI), including those caused by MRSA, and community-acquired bacterial pneumonia (CABP).¹⁸

Beta-lactam antibiotics include penicillins, aminopenicillins, cephalosporins and carbapenems. Their mechanism of action involves inhibiting the synthesis of bacterial cell walls by binding to penicillin-binding proteins (PBPs). Ceftaroline is unique in its ability to bind with high affinity to PBP2a, which is encoded for by a gene within MRSA.¹⁹ Multi-drug resistant organisms are growing in frequency; MRSA infections are not only becoming more prevalent in the hospital but also becoming increasingly challenging to treat. According to the Centers for Disease Control and Prevention (CDC), approximately 19,000 deaths occur annually because of severe MRSA infections. The standard first-line treatments for MRSA infections include vancomycin and linezolid. There is, however, growing resistance of *Staphylococcus aureus* to vancomycin with the development of vancomycin-intermediate and vancomycin-resistant *Staphylococcus aureus* (VISA and VRSA, respectively). Linezolid is bacteriostatic, as opposed to bactericidal, and associated with adverse side effects such as thrombocytopenia.²⁰ Therefore, ceftaroline is an antibiotic that appears to be able to fill an emerging need.

Ceftaroline antimicrobial spectrum includes much more than just MRSA coverage. Considered a broad spectrum agent, ceftaroline is active against many gram-positive as well as gram-negative organisms (see Table 2). Activity against *Methicillin-susceptible staphylococcus aureus* is greater than previous cephalosporins, with MIC90 multiple-fold lower than third generation cephalosporins. In terms of gram-negative coverage, ceftaroline is active against *H. influenza*, *E. coli* and nonextended spectrum beta lactamase-producing *Klebsiella*. It is important to note that this antibiotic does not cover *Pseudomonas aeruginosa* and there is limited data regarding activity against anaerobes.²¹

Table 2. Ceftaroline *In Vitro* Activity

<p>Skin Infections</p>	<p>Gram-positive bacteria</p> <ul style="list-style-type: none"> • <i>Staphylococcus aureus</i> (including methicillin-susceptible and -resistant isolates) • <i>Streptococcus pyogenes</i> • <i>Streptococcus agalactiae</i> <p>Gram-negative bacteria</p> <ul style="list-style-type: none"> • <i>Escherichia coli</i> • <i>Klebsiellapneumoniae</i> • <i>Klebsiellaoxytoca</i>
<p>Community-Acquired Bacterial Pneumonia (CABP)</p>	<p>Gram-positive bacteria</p> <ul style="list-style-type: none"> • <i>Streptococcus pneumoniae</i> • <i>Staphylococcus aureus</i> (methicillin-susceptible isolates only) <p>Gram-negative bacteria</p> <ul style="list-style-type: none"> • <i>Haemophilusinfluenzae</i> • <i>Klebsiellapneumoniae</i> • <i>Klebsiellaoxytoca</i> • <i>Escherichia coli</i>

There are currently no clinical drug-drug interaction studies conducted with ceftaroline and there were no clinically relevant changes in exposure to the antibiotic when medications affecting the cytochrome P450 iso-enzymes were administered concurrently according to phase II and III trials.²² The most common adverse events associated with ceftaroline were nausea, diarrhea and headache. Warnings and precautions are standard, including risk of hypersensitivity reactions and the need to inquire about patient history regarding beta-lactam allergies. There is also a warning regarding *Clostridium difficile* -associated diarrhea (CDAD), which is to be expected with broad-spectrum antibiotics.²³

Ceftaroline is available as an intravenous formulation and is dosed at 600 mg IV every 12 hours. Dose adjustments are necessary in patients with renal impairment (see Table 3). Ceftaroline is available in 400 mg and 600 mg vials of sterile powder for reconstitution in 20 mL sterile water, which is then further diluted. The formulation is compatible with normal saline, 0.45% sodium chloride solution, 5% and 2.5% dextrose solutions, and Lactated Ringer’s solution. The solution is stable for six hours at room temperature and 24 hours if refrigerated.²⁴

Table 3. Dosage Adjustments for Patients with Renal Impairment Adapted from TEFLARO® (ceftaroline) Highlights of Prescribing Information

Estimated Creatinine Clearance (mL/min) using Cockcroft-Gault formula	Recommended Dosage Regimen
<p style="text-align: center;">> 50</p>	<p style="text-align: center;">600 mg IV (over one hour) every 12 hours <i>No dosage adjustment necessary</i></p>
<p style="text-align: center;">> 30 to ≤ 50</p>	<p style="text-align: center;">400 mg IV (over one hour) every 12 hours</p>
<p style="text-align: center;">≥ 15 to ≤ 30</p>	<p style="text-align: center;">300 mg IV (over one hour) every 12 hours</p>
<p style="text-align: center;">End-stage renal disease (ESRD), including hemodialysis</p>	<p style="text-align: center;">200 mg IV (over one hour) every 12 hours</p>

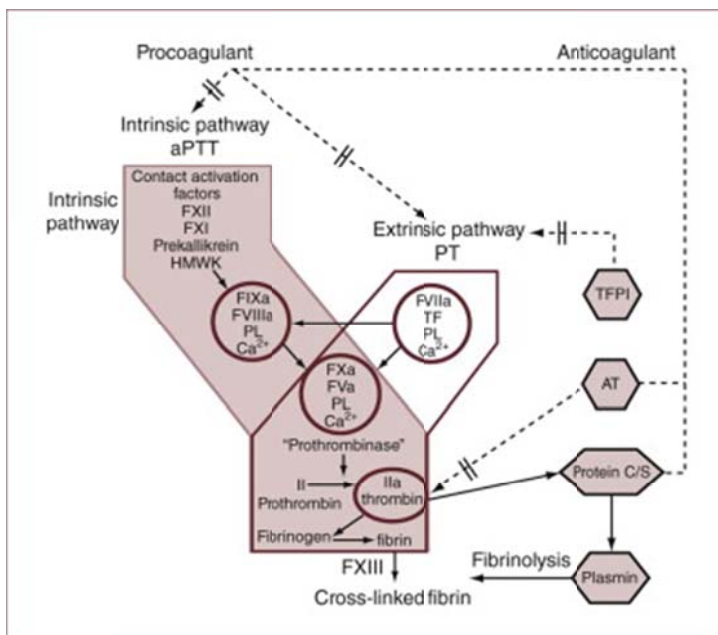
Agents Approved by the Food and Drug Administration in 2011

Rivaroxaban (Xarelto™)

Rivaroxaban is the first oral anticoagulant that targets coagulation factor Xa indicated for deep vein thrombosis (DVT) prophylaxis in patients undergoing hip or knee arthroplasty. The manufacturer is currently seeking additional indications, including stroke prophylaxis in patients with atrial fibrillation following clinically successful results in the ROCKETAF trial. It is also being studied for venous thromboembolism (VTE) treatment and secondary prevention (EINSTEIN); prevention of VTE in hospitalized medical patients (MAGELLAN); and secondary prevention of cardiovascular events in acute coronary syndrome patients.^{25,26, 27, 28}

There are four efficacy and safety studies that evaluated rivaroxaban as DVT prophylaxis in knee and hip replacement surgeries (the RECORD 1-4 trials). Each of these compared rivaroxaban with enoxaparin 40 mg daily or 30 mg twice daily. RECORD 1 and RECORD 2 studied rivaroxaban in hip replacement surgery while RECORD 3 and RECORD 4 studied rivaroxaban in total knee replacement. Each trial reported successful results, with a relative risk reduction for venous thromboembolism ranging from 31 percent (RECORD 4) to 88 percent (major VTE in RECORD 1). A pooled comparison of results of all four trials also demonstrated comparable bleeding risks and hemorrhagic complications between the rivaroxaban treatment arms and the enoxaparin treatment arms.²⁹

Factor X is a member of the common pathway of the coagulation cascade. It is the target of many anticoagulants, including vitamin K antagonists (warfarin), heparins and factor X inhibitors (fondaparinux). Activated factor X complexes with clotting factor V to cleave prothrombin to thrombin. Antagonism of factor X inhibits clotting by interrupting the cascade at this step. While fondaparinux (Arixtra™) indirectly inhibits factor X, rivaroxaban is a direct inhibitor of activated factor X. A competing oral Xa inhibitor, apixaban (Eliquis™), not yet FDA approved, is currently in development.



Rivaroxaban is indicated for once daily dosing (refer to Table 4 for dosing information). It is well absorbed (80-100 percent oral bioavailability) and is greater than 90 percent protein bound. It is also hepatically metabolized and undergoes renal elimination through tubular secretion. Other agents should be selected in patients with moderate or severe hepatic dysfunction. Caution should be exercised in patients with renal insufficiency and other anticoagulants selected in renal failure (calculated creatinine clearance < 10 mL/min). Rivaroxaban is not recommended for use in pregnant or nursing mothers.³⁰

As with other anticoagulants, patients on rivaroxaban should be cautioned to watch for signs of excessive anticoagulation. These include bruises that spread or do not heal within a normal period of time, blood in stool, or gum bleeds after oral hygiene that persist. There is currently no recommended monitoring of rivaroxaban, although chromogenic anti Xa levels can be assessed. In patients who may pose higher bleeding risk, such as patients with renal or hepatic insufficiency, ongoing monitoring of anti Xa levels may be advisable. Patients should be advised to alert their physician that they are using rivaroxaban prior to any invasive medical procedure.

Table 4. Dosing Information for Rivaroxaban

Indication	Recommended Dosage Regimen
Total Knee Replacement	10 mg once daily for 14 days following surgery
Total Hip Replacement	10 mg once daily for 35 days following surgery

Fidaxomicin (Dificid™)

Fidaxomicin is a narrow-spectrum macrocyclic antibiotic that represents a new class of antibacterial agents able to inhibit bacterial RNA polymerase.³¹ It offers another option for the treatment of *Clostridium difficile*-associated diarrhea (CDAD) and is unique in its ability to cover hyper-virulent strains that frequently lead to treatment failures.³² Fidaxomicin has been under investigation for the past 30 years. It was first discovered in the 1970s and was initially named lipiarmycin. It has since been investigated by various pharmaceutical companies for various indications under various names. In 2009, it was officially named fidaxomicin, and not until 2011 was it given FDA approval for the treatment of CDAD.

Clostridium difficile is a gram-positive anaerobe that is able to form spores and is responsible for 20-30 percent of all antibiotic-associated diarrheas. Before 2000, *C. difficile* infections were primarily found in the hospital setting and among older adults. Recently, more virulent strains have developed such that *C. difficile*-associated infections have increased in prevalence as well as mortality (mortality increasing from 2 percent to more than 10 percent in recent years).³³ Current treatment options according to Society for Healthcare Epidemiology of America (SHEA) and the Infectious Diseases Society of America (IDSA) clinical practice guidelines for *Clostridium difficile* infection in adults for CDAD include oral vancomycin and metronidazole; however, oral vancomycin is the only FDA-approved treatment. Metronidazole is considered first-line for mild-to-moderate CDAD due to its comparable efficacy and the potential for the development of vancomycin-resistant enterococci with use of vancomycin. Oral vancomycin is reserved for patients with severe/recurrent CDAD.^{34,35}

Fidaxomicin is active against gram-positive aerobes and anaerobes without any activity against gram-negative bacteria. This lack of gram-negative activity has been hypothesized to minimize the effects of the antibiotic on intestinal colonization and thus protect against colonization with *C. difficile*.³⁶ Fidaxomicin has been shown to have increased *in vitro* activity (approximately eight

times) against hyper-virulent isolates when compared to oral vancomycin. Also, in a recently published study in the *New England Journal of Medicine*, fidaxomicin was found to be noninferior when compared to oral vancomycin with respect to clinical cure rate and there were significantly less recurrences of infection in the fidaxomicin group.³⁷

Fidaxomicin is available as an oral tablet and is dosed as twice-daily for 10 days. There are currently no contraindications. Warning/precautions focus on the fact that it is not to be used for systemic infections due to its minimal systemic absorption. Fidaxomicin should only be used for its labeled indication because of lack of established benefit for other indications as well as the risk of development of drug-resistant bacteria.³⁸ The lack of adverse events, drug-interactions and convenient twice-daily oral dosing make fidaxomicin an appealing alternative to current agents used in CDAD, especially upon recurrence when hyper-virulent strains are suspected.

Table 5. Cost of Therapy of Agents for the Treatment of CDAD³⁹

Drug	Usual Dosing Regimen	Cost per Dose (AWP)	Cost per Treatment (AWP)
Metronidazole	500 mg orally three times a day for 10-14 days	\$0.73 (generic)	\$21.90 (10 days) \$30.66 (14 days)
Vancomycin (VancocinHCl) Capsules	125 mg orally four times daily for 10-14 days	\$31.83	\$1,273 (10 days) \$1,782 (14 days)
Fidaxomicin (Dificid)	200 mg orally twice daily for 10 days	\$168	\$3,360

Belimumab (Benlysta™)

Belimumab is indicated for the treatment of adult patients with active, autoantibody-positive systemic lupus erythematosus (SLE) who are already receiving standard therapy.⁴⁰ Standard therapy consists of corticosteroids, antimalarial agents, nonsteroidal anti-inflammatory drugs (NSAIDs), and immunosuppressive drugs alone or in combinations.⁴¹ Belimumab is the first new treatment approved for SLE in almost 50 years and is the first biological treatment targeted at the disease state (as opposed to supportive treatment).⁴²

SLE is a multi-system autoimmune disorder mediated by tissue-binding autoantibodies and immune complexes. Through interactions between susceptible genes and the environment, abnormal immune responses develop, such as reduced clearance of apoptotic cells and immune complexes and production of self-antigens and autoantibodies. The sustained production of autoantibodies and immune complexes bind to target tissues causing the activation of the complement system and immune cells, leading to the release of chemotaxins, cytokines and destructive enzymes. There is also an overexpression in B lymphocyte stimulator, which is a key survival cytokine for cells. The most common autoantibody produced is anti-nuclear antibodies (which also offer the best screening test), followed by anti-double stranded DNA.

SLE can involve several different organ systems and range in severity. Most patients experience exacerbations and periods of remittance but permanent remission (defined as the absence of systems and no need for treatment) is rare. Systemic symptoms include fatigue, myalgia and arthralgia.⁴³ B lymphocyte stimulator (BLyS) is a protein that functions as a cell mediator and is part of the tumor necrosis factor ligand super family. BLyS is present in two forms – soluble and membrane-bound. The soluble form is the active form, cleaved from the cell membrane and able to attach to three different receptors, which are largely expressed on B lymphocytes. When bound to these receptors, BLyS inhibits apoptosis and contributes to proliferation and differentiation of B lymphocytes into immunoglobulin-producing plasma cells. In SLE, increased BLyS levels are correlated with increased disease activity.⁴⁴

As mentioned, most therapies used in treating SLE are not targeted at the underlying immune disorder, but rather are supportive in nature. They target nonspecific sites of inflammation (nonsteroidal anti-inflammatories, antimalarial agents) and general immune suppression (corticosteroids, azathioprine, cyclophosphamide, methotrexate, mycophenolate).⁴⁵ Belimumab is a fully human immunoglobulin G1 lambda monoclonal antibody that is specific for the soluble form of BLyS and inhibits its biological activity. By doing so, it is able to selectively reduce the number of CD20+ B cells and plasma cells, and anti-double stranded DNA titers in patients with SLE.⁴⁶

In two clinical trials, BLISS-52 and BLISS-76 (52 and 76 weeks of follow-up respectively), 1,684 patients with active SLE were randomized to receive either IV placebo 1 mg/kg or 10 mg/kg Belimumab in addition to their current therapy. The primary endpoint for both trials was improvement in the SLE Responder Index. In both trials, significantly more patients in the Belimumab trial achieved response and had fewer disease flares. One of the main limitations of these studies is the small number of African American patients (where SLE is more common) and the fact that these patients did not appear to benefit from treatment with belimumab.⁴⁷

Belimumab is administered via intravenous infusion with a recommended dosage regimen of 10 mg/kg at two-week intervals for the first three doses, and then four-week intervals thereafter. The most common adverse effects reported include nausea, diarrhea and fever. The only current contraindication is in patients who have previously experienced anaphylaxis with belimumab.⁴⁸

Continuing Education Information

Important Information Regarding Continuing Education Credit

Due to new guidelines established by Accreditation Council for Pharmacy Education (ACPE), certain changes must be made to the process by which MPA accredits continuing education for pharmacy technicians. MPA may choose to designate programs or home study articles as PTCE-accredited, rather than ACPE-accredited.

However, even though MPA may accredit a program for technicians, it is the technician's responsibility to determine whether the subject matter is acceptable to the Pharmacy Technician Certification Board (PTCB) for recertification. Programs designated by PTCB to be appropriate for technicians pertain to the following topics: medication distribution and inventory control systems, pharmacy administration and management calculations, programs specific to pharmacy technicians, interpersonal skills, organizational skills, pharmacy law and pharmacology/drug therapy. Programs relating to functions outside the scope of practice for pharmacy technicians will not be accepted by PTCB.

This is a knowledge-based activity.

PTCE



Michigan Pharmacists Association is an approved provider of Pharmacy Technician Continuing Education (PTCE). PTCE Program #112-000-11-988-H01-T, 1.0 contact hour. Initial release date: 11/5/2011, Expiration date: 11/5/2014.

Michigan Pharmacists Association is accredited by the Accreditation Council for Pharmacy Education (ACPE) as a provider of continuing pharmacy education. ACPE Program #112-000-11-009-H01-P, 1.0 contact hour. Initial release date: 11/5/2011, Expiration date: 11/5/2014.

- The passing score on each test is 70 percent. Upon successful completion of the test, MPA will mail you a continuing education statement of credit. A failed test may be retaken only once without additional cost within 30 days upon notification of a failing score. There are no refunds for failed tests.
- The quiz may be taken any time until Nov. 5, 2014. Membership status will be certified using MPA records.
- This article offers 1.0 contact hour of continuing education. This lesson was developed specifically for pharmacists and certified pharmacy technicians.
- To complete the posttest and evaluation, you must complete this online form and process payment: MichiganPharmacists.org/education/online/posttest/
- For questions regarding continuing education, please contact MPA Director of Continuing Education [Mary Farrington](mailto:Mary.Farrington@mpa.org) at (517) 377-0234. For questions regarding the Web site and Internet requirements, please contact MPA Director of Communications [Leah Godzina](mailto:Leah.Godzina@mpa.org) at (517) 377-0232.

Posttest Questions

- Which of the following statements is false regarding dabigatran?
 - It is the first FDA-approved oral anticoagulant since warfarin
 - It is approved for all types of atrial fibrillation
 - It is not to be used in patients on dialysis
 - There is no specific reversal agent or antidote
 - More than one of the above is true
- Dabigatran is associated with more GI bleeding and dyspepsia than warfarin.
 - True
 - False
- Ceftaroline covers all except:
 - MRSA.
 - MSSA.
 - pseudomonas.
 - E. coli.
- The FDA-approved medication for *C. difficile*-associated diarrhea is:
 - Oral vancomycin.
 - Metronidazole.
 - Fidaxomicin.
 - All of the above
 - Two of the above
- Why advantage does fidaxomicin offer over current agents used for treating CDAD?
 - More convenient dosing regimen
 - Less recurrence of *C. difficile*-associated diarrhea
 - More cost effective
 - Less adverse events
 - More than one of the above
- Belimumab is used to decrease inflammation in patients with all types of lupus.
 - True
 - False
- Fingolimod acts at:
 - T cells
 - Oligodendrocytes
 - The blood/brain barrier
 - None of the above
 - All of the above
- In the FREEDOMS and TRANSFORMS trials, Fingolimod reduced multiple sclerosis relapse flares by
 - 20-30 percent
 - 30-40 percent

- c. 40-50 percent
 - d. 50-60 percent
 - e. 60-100 percent
9. Rivaroxaban acts by inhibiting:
- a. Vitamin K
 - b. Thrombin
 - c. Clotting Factor X
 - d. Clotting Factors II, VII, IX and X
 - e. Heparin
10. Rivaroxaban has an FDA-approved indication for which of the following?
- a. DVT prophylaxis in knee and hip arthroplasty
 - b. DVT treatment in symptomatized venous thromboembolism
 - c. DVT prophylaxis in atrial fibrillation
 - d. DVT prophylaxis in stroke patients
 - e. All of the above

Appendix A – Food and Drug Administration’s List of Novel Drug Approvals for 2010⁴⁹

Drug Name	Active Ingredient	Approval Date	Indication(s)
Eribulinmesylate	Eribulinmesylate	11/15	Indicated for the treatment of patients with metastatic breast cancer who have previously received at least two chemotherapeutic regimens for the treatment of metastatic disease
Egrifta	Tesamorelin	11/10	Indicated for the reduction of excess abdominal fat in HIV-infected patients with lipodystrophy
Teflaro	Ceftaroline fosamil for injection	10/29	Indicated for the treatment of acute bacterial skin and skin structure infections and community-acquired pneumonia
Lurasidonehcl	LurasidoneHCl	10/28	Indicated for the treatment of schizophrenia in adults
Pradaxa	Dabigatran etexilate mesylate	10/19	Indicated to reduce the risk of stroke and systemic embolism in patients with nonvalvular atrial fibrillation
Gilenya	FingolimodHCl oral capsules	09/21	Indicated for the treatment of patients with relapsing forms of multiple sclerosis to reduce the frequency of relapses and to delay the accumulation of physical disability
Krystexxa	Pegloticase	09/14	Provides for the treatment of intravenous infusion intended for patients with treatment failure gout to control hyperuricemia and manage the signs and symptoms of gout
Jevtana	Cabazitaxel	06/17	Indicated for the treatment of patients with hormone refractory metastatic prostate cancer previously treated with a docetaxel-containing treatment regimen
Prolia	Denosumab to	06/01	Provides treatment for prevention of osteoporosis in postmenopausal women
Natazia	Estradiolvalerate/dienogest tabs	05/06	Indicated for prevention of pregnancy
Asclera	Polidocanol	03/30	Indicated to treat uncomplicated spider veins (varicose veins less than or equal to 1 mm in diameter) and uncomplicated reticular veins (varicose veins 1-3 mm in diameter) in the lower extremity
Carbaglu	Carglumic acid	03/18	Indicated for use in pediatric and adult patients as an adjunctive therapy for the treatment of acute hyperammonemia due to nags deficiency, and as maintenance therapy for chronic hyperammonemia due to nags deficiency
Xiaflex	Clostridial Collagenase	02/02	Provides treatment of advanced Dupuytren's Disease
Victoza	Liraglutide	01/25	Indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus
Ampyra	Dalfampridine	01/22	Indicated to improve walking ability in patients with multiple sclerosis (MS)
Actemra	Tocilizumab	01/08	Provides treatment for reducing signs and symptoms in adult patients with moderately to severely active RA

Appendix B – Food and Drug Administration’s List of Novel Drug Approvals for 2011⁵⁰

Drug Name	Active Ingredient	Approval Date	Indication(s)
Xalkori	crizotinib	08/26	To treat patients with late-stage (locally advanced or metastatic), nonsmall cell lung cancers (NSCLC) who express the abnormal anaplastic lymphoma kinase (ALK) gene
Firazyr	icatibant	08/25	For the treatment of acute attacks of a rare condition called hereditary angioedema (HAE) in people ages 18 years and older
Adcetris	brentuximabvedotin	08/19	For the treatment of Hodgkin lymphoma and systemic anaplastic large cell lymphoma (ALCL)
Zelboraf	vemurafenib	08/17	To treat patients with late-stage (metastatic) or unresectable (cannot be removed by surgery) melanoma, the most dangerous type of skin cancer
Brilinta	ticagrelor	07/20	To reduce cardiovascular death and heart attack in patients with acute coronary syndromes (ACS)
Xarelto	rivaroxaban	07/01	To reduce the risk of blood clots, deep vein thrombosis (DVT) and pulmonary embolism (PE) following knee or hip replacement surgery
ArcaptaNeohaler	indacaterol inhalation powder	07/01	For long-term, once-daily maintenance and bronchodilator treatment of airflow obstruction in people with chronic obstructive pulmonary disease (COPD), including chronic bronchitis and/or emphysema
Nulojix	belatacept	06/15	To prevent acute rejection in adult patients who have had a kidney transplant
Potiga	ezogabine	06/13	For use as an add-on medication to treat seizures associated with epilepsy in adults
Dificid	fidaxomicin	05/27	For the treatment of <i>Clostridium difficile</i>-associated diarrhea (CDAD).
Incivek	telaprevir	05/23	To treat certain adults with chronic hepatitis C infection
Edurant	rilpivirine	05/20	For the treatment of HIV-1 infection in adults who have never taken HIV therapy
Victrelis	boceprevir	05/13	To treat certain adults with chronic hepatitis C
Tradjenta	linagliptin	05/02	An adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus
Zytiga	abiraterone acetate	04/28	In combination with prednisone (a steroid) to treat patients with late-stage (metastatic) castration-resistant prostate cancer who have received prior docetaxel (chemotherapy)
Vandetanib	vandetanib	04/06	To treat adult patients with late-stage (metastatic) medullary thyroid cancer who are ineligible for surgery and who have disease that is growing or causing symptoms
Horizant	gabapentin enacarbil	04/06	A once-daily treatment for moderate-to-severe restless legs syndrome
Yervoy	ipilimumab	03/25	To treat patients with late-stage (metastatic) melanoma, the most dangerous type of skin cancer
Gadavist	gadobutrol	03/14	For use in patients undergoing magnetic resonance imaging (MRI) of the central nervous system

Benlysta	belimumab	03/10	To treat patients with active, autoantibody-positive lupus who are receiving standard therapy - corticosteroids, antimalarials, immunosuppressives and nonsteroidal anti-inflammatory drugs
Daliresp	roflumilast	02/28	To decrease the frequency of flare-ups (exacerbations) or worsening of symptoms from severe chronic obstructive pulmonary disease (COPD)
Edarbi	azilsartanmedoxomil	02/25	To treat high blood pressure (hypertension) in adults
Viibryd	vilazodone hydrochloride	01/21	To treat major depressive disorder in adults
Natroba	spinosad	01/18	For the treatment of head lice infestation in patients ages four years and older
Datscan	ioflupane i-123	01/14	An imaging drug used to assist in the evaluation of adult patients with suspected Parkinsonian syndromes (PS)

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